JANUARY, 1950

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

Corticodiencephalic Gastrointestinal Syndromes in Epileptics

Observations on an Isolated Gastric Pouch in Man

Fissure-in-Ano

Fifteenth Annual Convention

New York, N. Y., 9, 10, 11 October 1950

VOLUME 17 NUMBER 1

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

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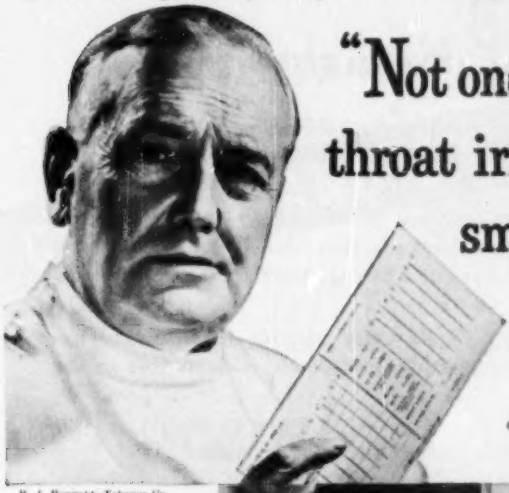

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The Review of Gastroenterology

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Volume 17 JANUARY, 1950 Number 1

CORTICODIENCEPHALIC GASTROINTESTINAL SYNDROMES IN EPILEPTICS*

(Part I)

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Introduction

Gastrointestinal motor and secretory functions have not as yet been fully localized in fibre tracts and centers of the nervous system as well as the motor and sensory and other functions. For this reason the vomiting of central origin that one observes in cases of brain tumor, brain abcess, and meningitis forms a subject of great interest. The neurologist often encounters vomiting at the onset of diseases such as poliomyelitis, encephalitis, cerebral vascular accidents, uremic coma, sinus thrombosis, as well as other conditions such as intracranial injuries. It, therefore, needs more definite localization to be of diagnostic value than merely the statement that it may be of cerebral, mesencephalic or of pontobulbar origin. Aside from the descriptions of scattered gastrointestinal syndromes that one sees here and there in the course of descriptions of certain combinations such as uncinate fits, there is very little elaboration of the representation of the stomach, intestines, and related organs within the cerebral hemispheres for the gastroenterologist's use in the great collection of problems that confront him in his practice. The subject of supramesencephalic localization of gastrointestinal functions has become of increasing importance in recent years with the production of stomach and duodenal ulcers in the course of experimental researches in the hypothalamus and related centers.

Although some advances have been made in the experimental investigation of centers of gastrointestinal function in the course of nonepileptic experimental investigation and, to a somewhat greater extent on a clinical basis, little has been

*Read in part before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.

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done on this subject in epilepsy. Experiments dealing with vomiting, intestinal contractions and secretory functions in the course of convulsions have been covered in only a few phases. It is surprising to know that clinical research on the gastrointestinal system has been covered in only about ten papers in which the subject of convulsions has been under investigation. In presenting our material we will therefore give a detailed description of work that has thus far been done on the clinical, x-ray, and laboratory procedures used to investigate the disturbances in function of the stomach, intestines and related organs in epileptics. This will be followed by a detailed description of experimental data dealing with stimulation of various portions of the cerebrum including the cortex of the brain and its effect on the motility of the stomach and the small as well as the large intestines in nonconvulsives. Since the bulk of experiments dealing with the above system involved stimulation of various parts of the diencephalon, a greater emphasis will be assigned to some of the outstanding papers on this subject. In this respect we will cover, in nonepileptics, the data dealing not only with such reactions as vomiting, salivation, contraction of the stomach and intestines, but also with upsets in the control of water metabolism and cerebral control of urinary bladder function. This is necessary, since in our cases we often note an aura of vomiting to be associated with thirst and dryness in the mouth and sometimes with preparoxysmal urination.

It becomes evident that whether we deal with the gastrointestinal tract in relation to convulsions or otherwise, little of an important nature has been done with experimental and clinical material as far as the representation in the brain is concerned. Although many experimentalists have discovered a great deal on this subject with regard to localization in the brain stem and in the mesencephalon and even in the hypothalamus, many of the facts and experimental results seem contradictory. In spite of the above, much of the material has a solid foundation. In fact many of the chemical and electrical stimulations of some of the brain centers resulted in an abundance of motor as well as sensory symptoms that were specifically gastrointestinal. Along an anatomical line the subject of gastrointestinal representation within the diencephalon as well as in the telencephalon also creates a problem which needs much clarification. This is necessary since some authorities seem to insist that only one tract, center or pathway should represent the gastrointestinal system in the cerebrum. From the literature to be presented it will become evident that there are a number of pathways not only within the cerebral hemispheres but also in other portions of the brain that govern the motor as well as the secretory functions of the stomach and intestines. Although we will concentrate, in our anatomical descriptions, upon those fibres which lead from the anterior thalamic nucleus to the cerebral cortex and the connections with the mammillary bodies thus leading into the mesencephalon, we will also show that similar pathways are presented that carry the above functions. The anatomical data to be covered will be in the form of a figure resembling a basket on a tripod.

Following our anatomical descriptions we will dwell to some extent on the physiological material dealing with convulsions. This will be important since the

usual convulsion is associated with the activity of the autonomic nervous system in both gastrointestinal and nongastrointestinal manifestations.

The changes in the pupils, the pattern of attack consisting of movement of the head and eyes to the right or the left, as well as other features of a localizing nature within the brain offer another means of placing definite areas that control sympathetic as well as the parasympathetic functions. It has been shown by a number of authorities that a convulsion may occur with a simultaneous reaction of the parasympathetic as well as the sympathetic system. This is noted particularly in the convulsions with myosis resulting from stimulation by creatinin and picrotoxin and in those stimulated by absinthe and accompanied by mydriasis. In discussing the above subjects dealing with the mechanism of the convulsion in the light presented, it will become evident that the neurophysiology of the gastrointestinal tract in particular, as well as that of the autonomic in general, will be placed on a somewhat more workable basis. Following the above material, we will attempt to show that not only is it important to trace the brain centers dealing with the autonomic system on an experimental basis but that the clinical material such as observed in muscular wasting is also important. This is seen from the work of Archambault who attempted to trace the autonomic fibres which if diseased might produce facial atrophy. His work will therefore be referred to not only because of its data on the autonomic system bearing on the gastrointestinal muscular system but also because muscular atrophy is seen in many of our cases of epilepsy.

After acquainting the reader with sufficient experimental as well as clinical data pointing towards the existence of definite autonomic pathways in the cerebrum, both its telencephalic and diencephalic portions controlling activities of the gastrointestinal system, we will undertake the presentation of our material. Although we were forced in our anatomical references to discuss the autonomic system in general because of the meagre data which specifically pointed to the gastrointestinal system, a similar descriptive indulgence will be abandoned in the presentation of our cases. Only those patients who present definite gastrointestinal aurae such as vomiting, epigastric distress, belching, constipation, diarrhea, pain in all abdominal quadrants, hunger, thirst, etc. will be used for material. In addition to the segregation of our cases into syndromes, on the basis of the aurae mentioned above, emphasis will be placed upon such cases showing an aura of vomiting for instance, that is also accompanied by some other localizing manifestation. Cases which present the gastrointestinal aura associated with another aura pointing towards the occipital lobe for instance, will be placed in a different category from those of the frontal or temporal. Using the above method our material will be divided, according to the aura dealing with the gastrointestinal tract, into definite group and possibly lobar syndromes.

The cases falling into each group syndrome will then be classified according to their present residential and observational status at the institution. In the group of over 300 cases in whom the gastrointestinal aura are present, less than half of

the number had succumbed at the time that the study was made. Since a complete neurological workup on these patients was impossible, only the causes, the onsets and the duration of the epilepsy as well as other historical data dealing with the gastrointestinal tract symptoms will be presented. If autopsy material is available in the deceased cases such will be presented particularly if the same bears a relationship to the gastrointestinal aura. The living cases in these group syndromes will be analyzed for the causation, type of seizure, as well as the detailed neurological findings. The results obtained in the course of the usual neurological investigation will be presented. Items such as gait, coordination, muscle strength, as well as muscle atrophy will be dealt with. The last mentioned item however, will be given special consideration.

Wherever possible the phenomenon of neurosomatic deterioration in its mental and physical, and particularly its autonomic features will be stressed. The subject of neurosomatic deterioration has been of interest in many of the studies on epilepsy during the last decade. It is a phenomenon of massive body rigidity that occurs in a certain percentage of epileptics and in many of these cases it is associated with not only many features of autonomic imbalance, but also with mental deterioration. This deterioration, from the psychiatric view, consists of an emotional as well as an intellectual weakening. The rigidity is not unlike that seen in the terminal stages of diseases such as multiple sclerosis and encephalitis. The neurological examination will be followed in some cases by a description of the pneumoencephalographic findings. From the above it will be seen that if a lesion in an epileptic is localizable, then the accompanying gastrointestinal symptoms occurring with the attack should also be definitely localizable in the cerebral hemispheres.

Gastroenterology in Epilepsy

Some advances made in the field of endocrinology in the past two decades resulted in contributions in all fields. Knowledge of functions of the liver and pancreas in relation to the above and otherwise has been advanced. The study of the gastrointestinal system has thus profited and the reverberations of this progress resulted in advances in our knowledge of nutrition and metabolism in general. The synthesis of amino acids in the body is much better understood now than it ever has been before (Best and Taylor). Furthermore, the relationship between the amino acid metabolism and the vitamins has been developed to such a great extent that is can be put into a schematized system such as may be seen in the Krebs Cycle (Upjohn 1947), in which the relationship of most of these classes of substances to glucose and pyruvic acid is shown. Volumes can be written on the interrelationships between endocrinology, gastroenterology and metabolism and nutrition. Not only has there been even an insignificant attempt to study the nature of the above combined advances in relation to epilepsy but the ordinary physiologic principles or possibly pathologic disturbances in the gastrointestinal system have as yet not been even slightly placed on a recognizable plane in this

disease. The only reference to gastrointestinal systems in relation to the actual fit is noted in the form of aura as they appear in the literature under the heading of other subjects in epilepsy.

In 1931 one of us (Weingrow) presented some data on this subject of changes in the gastrointestinal system in direct relationship to fits produced in various animals by the injection of absinthe. Most of the material appearing in the literature deals largely with the observations of a clinical and laboratory nature made upon the gastrointestinal tract in epilepsy, none being of a motor and secretory nature.

Although the medical literature seems to be replete with material such as diet in causation of epilepsy (Tracy) it seems to us advisable to disregard subjects of this nature. In reviewing our 5,000 institutional cases we have noted many individuals upon admission to the institution with causes of epilepsy that were said to be related to diet. In some cases the eating of particular foods such as bananas, ripe fruit, pork, peanuts and many others were offered as causes. For self-evident reasons we have eliminated such cases from our consideration. Other material in the literature deals with such vague items as for instance intestinal origin of epilepsy (Baldwin). This may also be considered as unworthy of consideration. Occasionally one meets with definite organic disturbances such as obesity, epileptiform attacks and recurrent jaundice (Fearnsides). Even such material has been encountered in our institutional cases, but these we did not consider worthy of inclusion and we must therefore omit them from consideration of our work on epilepsy. A good percentage of our cases consisted of definite intestinal diseases such as typhoid or dysentery, but even this we felt unworthy of consideration because there was no definite evidence of brain involvement even though the epilepsy followed attacks of such diseases. We found a common item in the list of alleged causes of epilepsy which may be noted in the paper by Block. This deals with etiologic relationship of worms to epilepsy. Again, we felt that such material, though rather frequent, must be eliminated from our cases and therefore, deserves no consideration in this review of the literature.

Instead of dealing with the irrelevant in the literature, particularly the material on intoxication, we believe that emphasis on motor and secretory phenomena of the gastrointestinal system in relation to epilepsy is in order. Although in the last five years some rather comprehensive work has appeared on the subject of epilepsy, in none of these do we find material as suitable for our purpose as that which we see in the review of Lennox and Cobb (1929). For this reason, we think their data will be of much importance in relation to our subject. From their material it is evident that they agree with the opinions we have expressed in the foregoing.

These workers felt that abnormalities of the gastrointestinal tract have been frequently accused of playing a prominent part in seizures. Although they do not express their opinions in relation to the occurrence of inordinate appetites and constipation seen in epileptics, it seems that they do not feel that graduation of

the diet and the regulation of the bowels are a sufficient remedy for seizures. Indiscretions of the diet resulting in fits may be a concomitant symptom rather than a cause. Lennox and Cobb state that although most clinicians agree to the therapeutic importance of a normal functioning of the gastrointestinal tract in epilepsy, they differ widely in their statements concerning the incidence of the intestinal abnormalities and specific relation of such abnormalities to seizures. Little consideration is given by these investigators to those writers who believe that constipation is a result of the poor physical and mental condition of the epileptic patient. It is evident that there is nothing specific about the word "poor" whether in a physical or mental sense. Concrete data is important in scientific investigation according to these authors. For this reason Lennox and Cobb also dismissed work such as that done by Reeves (1921) on chronic convulsive toxemia of intestinal origin. These reviewers of the literature on gastrointestinal epilepsy found the subject of pathology rather than toxicology more interesting, as may be seen in the following.

Although Lennox and Cobb realized that the only possible importance of pathology of the gastrointestinal tract in epilepsy could be on a peripheral irritation basis, they nevertheless took pains to discuss the work of Caro as follows: "The available autopsy reports show a surprisingly small proportion of abnormalities. Caro (1917, a & b), in 280 autopsies of institutional cases found intestinal adhesions and peritoneal bands in 18 per cent. This was the same percentage found in 775 nonepileptic patients autopsied at the Boston City Hospital. Caro, concluded therefore that constipation in epilepsy is rarely due to congenital defect, but is due to the same causes as in other patients". Lennox and Cobb thought that the adhesions found were the result rather than the cause of the fits. As to adhesions both Caro as well as the writers reviewing his material must agree that mechanical, toxic, infectious, metabolic as well as neoplastic factors might be the responsible agents of this inflammatory process. Local hemorrhages such as occur during a convulsive episode may also cause the adhesions.

It is interesting to note that an author such as Lennox and a well known neuropathologist such as Cobb found the subject of observable organic changes in the gastrointestinal tract important in relation to convulsions. These authorities were probably interested in such findings not alone from the point of view of the causation of the convulsions on the basis only of peripheral irritation but also because of their interest in laboratory phenomena on which they have done a great deal of work in the field of epilepsy. If there is a disordered metabolism in epileptics is seems rational to deduce that such might be reflected in the motor as well as secretory functions of the gastrointestinal tract. These authorities may also be cited verbatim as follows: "We have tabulated data concerning certain abnormalities found in the 423 autopsies performed at Craig Colony. The percentages of certain lesions are as follows: Dilated stomachs 5 per cent; inflammations of the small intestine, nontuberculous 9 per cent; tuberculous 3 per cent; inflammation of the large intestines, nontuberculous 14 per cent; tuberculous 1 per

cent; enlarged mesenteric lymph nodes, nontuberculous 9 per cent; tuberculous 6 per cent." These investigators felt that if one may accept these routine autopsy reports, epileptic patients show no greater degree of organic abnormalities of the gastrointestinal tract than other types of institutional patients who have not been subject to convulsions. Here it may be relevant to remark that by institutional patients, Lennox and Cobb meant mental epileptic cases falling into the groups of psychotics or mental defectives. Such patients usually show involvements of the gastrointestinal tract because of vitamin deficiencies, disturbed appetites, or trophic phenomena incidental to organic or functional brain disease. If the reviewers had the above in mind, they were probably correct since, in epileptics, one finds appreciable mental deterioration as well as psychotics. These investigators were also correct in their criticism of Reed (1916a), who stated that 100 per cent of the operated cases presented dilations of the duodenum and enlarged retroperitoneal glands. This last mentioned authority looked for pathological material in the gastrointestinal system because he found a specific bacterium causing epileptic fits.

Although one does not completely agree with the statement of Lennox and Cobb, observation made at autopsy does not necessarily give information concerning the positions of the gastrointestinal tract during life. In data of intussusception one finds however a contradiction to the above. Lennox and Cobb's discussion of the functional disorders of the gastrointestinal tract deserves analysis. They state, for instance, that important information of the parts may be gained by x-ray examination. They furthermore mentioned the blanket statement of Reed (1921) that all epileptics in his 810 consecutive examinations show splanchnoptosis.

They cite the findings of Harryman & Donaldson (1923) on this subject. Of 50 patients examined by means of a barium meal, the following findings were made. Twenty-five of the patients had hypermotility, usually of the colon, 19 had a slight degree of stasis, and in none was there evidence of marked stasis. Two showed evidence of ulcers, one of ptosis, three of adhesions, and thirteen of chronic inflammation of the appendix. The reviewers proceed further into the subject of functional disorders of the gastrointestinal tract by analyzing the findings of Bethea (1927). He studied 400 institutional patients. Some of the abnormalities noted were, pyloric spasm, 25 per cent; dilated stomach, 28 per cent; spastic colon, 16 per cent; colonic stasis, 41 per cent; hypermotility of the small intestine, 40 per cent; spasticity, 42 per cent. At this point we feel that our painstaking scrutiny into the most minute and detailed statements made by the two outstanding neurologists brought us the conclusion we were seeking. They state: "These results are indicative of autonomic imbalance but need comparisons with similar data obtained from healthy persons": By autonomic they mean of course, organic or functional.

In their appraisal of the literature the investigating reviewers considered above seem to have failed to arrange the material on a paroxysmal and a nonparoxysmal basis. This is probably because they found little material of the former variety in the papers which they analysed. If an epileptic fit can be followed by a paralysis

of an extremity, hallucination, stupor, aphasia, positive Babinski and other reflexes, etc., it is reasonable to conclude that positive gastrointestinal findings may also occur during or after a fit. It is therefore not unlikely that, just as the manifestations of organic brain diseases which follow an epileptic fit clear up soon thereafter, some of the gastrointestinal motility and secretory changes do likewise and thereby elude observation.

Lennox and Cobb proceed to secretory data and give the following descriptions of the material on the subject. The first analysis of secretory gastrointestinal changes in epileptics was that of an investigation by Felsen. It seems that at that time this was the only work on an analysis of the gastric juices of epileptics. Lennox and Cobb claim that in 53 patients Felsen studied the acidity of the gastric juices following the ingestion of water. In 15 per cent there was absence of HCl. Some criticism is offered upon the selection of Felsen's control group. Upon the reading of his paper, it seems that he did mention an aura and interparoxysmal gastric symptoms. Felsen's investigations were stimulated largely by the fact that epigastric distress is a common symptom in many epileptics. It seems that the author further undertook this investigation because Brown-Sequard described a spinal form of epilepsy. Since the absence of free HCl is found in spinal disease, Felsen thought that such a condition might also be present in epileptics. He postulated that the lateral horn might be the seat of the pathology which produces gastric secretory dysfunction.

Lennox and Cobb wondered, whether Felsen's patients without free HCl had been on a meat free diet.

Constipation was the next subject considered by Lennox and Cobb. They stated that there is common agreement that epileptic patients are usually constipated. They felt that even such a simple statement as the above had not been verified by actual observation in a large series of cases. The work of Nielson (1925) upon 200 epileptics and an equal number of controls was mentioned. Eighty-seven per cent of idiopathic epileptics were constipated. Seventy-eight per cent of symptomatic patients were found constipated in comparison with non-epileptics in whom 66 per cent were found afflicted. The authors felt that Nielson was not specific in regard to the type of constipation. Lennox and Cobb elaborated very little on the work of Vining (1922). Out of 194 cases, one third presented a history of bilious attacks. Vining's cases seemed not to have been checked against a control group. It seems that particularly in this chapter of their book Lennox and Cobb were not too critical of the material presented since this was a compilation of data.

For some time before 1929 a number of authors investigating the tuber cinereum in epilepsy showed that there is a cerebral control of visceral functions. This is seen in the work of Morgan and Gregory (1930) and Morgan and Johnson (1930), that of the former being on idiopathic epileptics, and that of the latter on experimental animals. In 1928 Morgan investigated the tuber cinereum in relation to specific visceral functions. At that time and for a number of years there-

after he was particularly interested in the cellular configuration of the above mentioned structure as well as that of the region between it and the globus pallidus, fields of Forel, and the fibre tracts leading from the last mentioned structures along the lines of the ansa lenticularis down toward the posterior commissure. The above pathways as well as the mammilloinfundibular area, interested Morgan in relation to their control of certain special organs. He was of the opinion that tuber cinereum, connected in the manner described above, exerted influence upon the thyroid gland, the adrenal gland, and also regulated the motor activity of the intestinal canal, among other functions. It seems that facts such as the above, dealing with physiology of the autonomic, might be relevant in relation to the clinical material presented heretofore. Other specific data such as that shown by Muskens on the dilation of the pupil with camphor convulsions, the contraction of the pupil with creatinin convulsions (Furstner), and picrotoxin (Pollock) convulsions, would not be out of order in describing the sympathetic and parasympathetic nervous control of intestinal activity. However as may be seen from the following, Lennox and Cobb were more interested in clinical rather than in experimental material.

It seems that they finally encountered the material which they were seeking. In the work of the authors to be mentioned they found that motor disturbances in the gastrointestinal tract were related to some causative agent, since the removal of the cause reduced or even caused a disappearance of the epileptic attacks. This is seen in the reports of Robertson (1924), Barclay (1917), and Block (1923). In the cases of the above mentioned authors chronic intestinal stasis, when cured, resulted favorably for the epilepsy. Treatment with acidophilus milk was favorable in the report of Axtell (1916). Good results were also obtained in the surgical correction of the effects of gastrointestinal toxemia, according to Armstrong (1926), and Brewster (1922). Although Lennox and Cobb felt that the reports upon disturbances in the structure and function of the liver were inconclusive in epileptics, they nevertheless mentioned the work of the following. At Craig Colony 423 autopsies were accompanied by atrophy of the liver in 9 per cent, hypertrophy in 2 per cent, fatty liver in 17 per cent, adhesions about the gallbladder in 4 per cent, and cholelithiasis in 5 per cent of the cases. In relation to the above they report the work of Thom (1916), Lalor and Haddon (1920), and finally that of Lind (1926). Reports of results with surgical interference were made by Reed (1916a-1920).

Rather than spend more time on the analysis of other texts on this subject we feel that the direct quotation from Lennox and Cobb will cover epilepsy in relation to the gastrointestinal tract. This will furthermore explain our adherence to the type of material which we selected. The summary of Lennox and Cobb is as follows: "A widespread belief that the gastrointestinal tract plays a prominent role in seizures is not supported by convincing data in the literature. Apparently organic or functional abnormalities are not more common in epileptic than in other nervous patients. We are without direct evidence of a toxic substance arising in the intestines that may contribute to seizures. Presumably distention of the colon may cause nerve fatigue by overstimulation of sensory nerves or it may be that

the effect is due simply to the general physical fatigue and lowered physical fitness which oftentimes accompanies constipation". With the above analysis and quotations from the literature we feel that the clinical material dealing with the motor and with the secretory features of gastroenterology in relation to epilepsy has been covered. We realize, however, that Lennox and Cobb have no particular interest in the exclusive research features of the subject of gastroenterology any more than they have in elaborating upon special problems of a subject such as electrolyte function in epilepsy. We therefore consider the above quotation sufficient and we will not go further to present the data which these authors have offered on the bacteriology of blood and feces. We will therefore depart from the above to consider the subject of nervous mechanism of the stomach and intestines as governed by the cerebrum.

Having presented the above data we, as students of epilepsy, feel rather discouraged over the fact that even with such little material someone with a neurophysiologic training did not grasp the opportunity to shed more light on the neurogenic control of the viscera in epileptics. We become more convinced that our attitude is correct when we find that Schiff, in 1867, noted gastrointestinal changes in cases of thalamic lesions. How much advantage the average neurologic clinician has taken of this discovery will be seen from the following pages.

Diencephalic Control of Gastrointestinal Activity in Nonepileptics

A detailed explanation of the mechanism of the production of motor and secretory changes in the gastrointestinal tract without the simultaneous occurrence of convulsions is necessary because of the paucity of such clinical and experimental data in epilepsy. Not only has the material in epilepsy been meagre but hardly any reference was made in the few observations heretofore presented to control of the stomach by either the cerebral cortex or the diencephalon. For this reason we shall proceed to present first our data on the diencephalic control of the gastrointestinal tract. This will then be followed by a much more detailed description of the results obtained by direct cortical stimulation. The reason for the greater detail of the latter will be found in the fact that it is important because convulsive phenomena are at present considered to be of corticogenic origin. Secondly because intensive research in cortical control of gastrointestinal movements has been started only a decade and a half ago by James Watts and needs continuation.

We are therefore forced to restrict ourselves to historical data and to the most essential facts in the form of short statements and references in dealing with the hypothalamic regulation of gastrointestinal activity. Here and there some allusions will be made referring to contraction of the bladder resulting in urination when the hypothalamus is stimulated. The discussion of hypothalamic influence on water regulation will be restricted almost completely to the mere mention of names while reviewing its literature. The last mentioned course is necessary because various aurae in the material which we hope to present consist of thirst, dryness of the mouth, sweating, diarrhea and other dehydration phenomena.

Despite the wealth of material concerning the hypothalamus accumulating daily, there is as yet insufficient well controlled experimental data with regard to its relationship to the gastrointestinal tract. Although many of the facts are contradictory, all that appears indisputable is the existence of some controlling influence from the hypothalamus on the muscular and secretory activity of the gastrointestinal tract. How this control is exerted, through what nuclear masses and fibre connections it becomes effected, is still disputed, and indeed there is too little data upon which we can rely with any degree of certainty. Figure 1 shows the horizontal level perpendicular to which later coronal figures are located.

Karplus and Kreidl (1909) were the first to show evidence of diffuse sympathetic activity resulting from stimulation of the hypothalamus. The direct effect

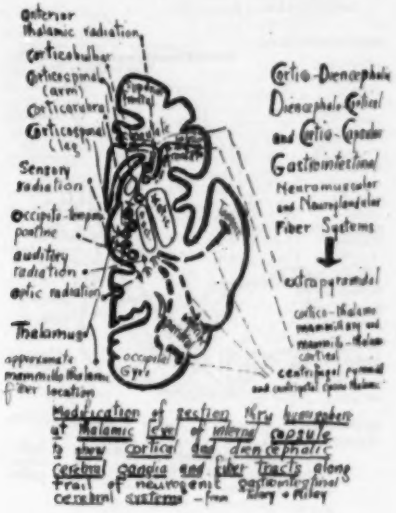


Fig. 1

of such stimulation upon the stomach and intestines was not obtained by them. Cushing (1931 and 1932a) actually introduced the relation of diencephalic structures to gastrointestinal activity when in a series of stimulating papers he reported pylorospasm, retrograde peristalsis, vomiting, and other manifestations of parasympathetic activity after injection of pituitrin or pilocarpine into the lateral ventricle of man. The monumental work of Beattie (1932a) then followed the above. In further work Cushing presented in a new light the evidence for a neurogenic factor in the etiology of peptic ulcer.

Experimental results on animals are complicated by the following facts. In the first place wall and sphincteric innervations vary in different animals. Furthermore, any nerve stimulated, whatever its anatomical designation, may contain both motor and inhibitory fibres to the gastrointestinal tract. Likewise, in stimula-

tion experiments of the central nervous system the effect may be the result of either motor or inhibitory impulses. One must, therefore, be cautious in interpreting the effects of stimulation as indicating the presence of a sympathetic or parasympathetic center. In presenting the following data, classification into motor and secretory reaction type will be followed by the effect of hypothalamic lesions on the anatomy and pathology (erosions and hemorrhages) of the gastrointestinal tract. The work on the effects of peripheral nerve stimulation as shown by McCrea, McSwiney and Stopford (1925), McCrea and McSwiney (1928), McSwiney (1931), Patterson and Rubright (1934) which led to our caution in the interpretation of results, was followed by the experiments of Beattie (1932a) who was the first to describe changes in the gastrointestinal activity following hypothalamic stimulation. In a later paper (1932a) he elaborated on the theory of an

Fig. 2

anteriorly placed parasympathetic center consisting of the supraoptic and tuberal regions and a posteriorly situated sympathetic center in the mammillary region of the hypothalamus. His work was repeated in 1934 (Beattie and Sheehan). The experiments showed that stimulation of the tuberal region resulted in a rise in intragastric pressure (accompanied by a fall in blood pressure), with a subsequent increase in peristaltic movements of the stomach. Stimulation of the posterior hypothalamus was followed by a slight fall in the intragastric pressure and obliteration of all gastric motility. The work of Kabat, Magoun, and Ranson (1935), Ranson and Magoun (1939), Rioch and Brenner (1938), gave the results of gastrointestinal as well as urinary bladder responses upon hypothalamic stimulation. The urinary part was obtained in the experiments of the last mentioned two authors. The above authors as well as Clark (1938), stressed the

sudden change while stimulating in passing from the supraoptic to the tuberal portions of the hypothalamus. Posterior to this and particularly in the lateral hypothalamic area numerous points were located which yielded vigorous sympathetic responses. Division into sympathetic and parasympathetic types of response in any one of the above specified regions was shown to be inconsistent by the results of Crouch and Eliott (1936), Ectors (1937), Ectors, Brookens and Gerard (1938), Hess (1936), Stavraky (1936), von Bogaert (1936) and Masserman and Haertig (1938). Although it is claimed by Sheehan that the last mentioned authors dealt with the gastrointestinal tract, a review of Stavraky's paper shows repeated reference to salivation, other autonomic reactions as well as convulsions in addition to gastrointestinal response. Figure 3 shows anatomical and historical data.

Fig. 3

Sheehan, in discussing the results of Masserman and Haertig stated that the difference in results upon the gastrointestinal tract obtained in the various portions of the hypothalamus by these authors as compared with those encountered in the experiments of others was probably due to the variation in the strength of the stimulating current, etc.

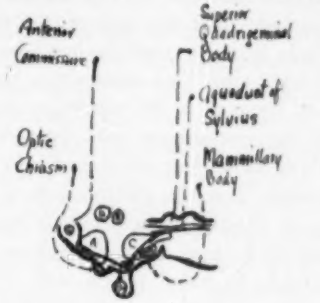
Sheehan terminated the data on motor manifestations of stimulation by stating that Beattie and Sheehan (1932) noticed that the motor responses of the gut followed "anterior hypothalamic" stimulation after a period sometimes as long as thirty seconds, whereas the sympathetic discharge from "posterior hypothalamic" stimulation follows almost immediately with a short latent period of approximately one second (Ranson and Magoun—1939). Sheehan finally states that it is strange that the effects on the colon and rectum have not yet been investigated, particularly

since the clinical importance of the nerve supply to the large bowel has been recently emphasized in the reported results of lumbar sympathectomy and spinal anethesia for megacolon [Stabins, Morton and Scott (1935); Telford (1939)].

The conclusions reached by Sheehan consist of the following very important facts: All observers agree that adequate stimulation of the hypothalamus, particularly in the posterior part of the lateral hypothalamic area, is followed by inhibition of peristalsis and diminished muscle tone in the stomach. It has been shown that there is, in addition, an increase in the mucus content of the gastric juice and a tendency to diminish its rate of flow. Although autonomic reactions following hypothalamic stimulation can still be elicited after removal of the adrenal glands and pituitary body (Karplus and Kreidl—1927) such experiments have not yet been applied to the gastrointestinal responses. Nevertheless, taking other preceding facts of hypothalamic stimulation into consideration, there are adequate grounds for accepting a sympathetic center regulating gastrointestinal activity, located in the hypothalamus, more particularly in the lateral hypothalamic area. The evidence does not warrant a more exact anatomical localization, although the posterior (mammillary) region appears to be particularly responsive. It must be remembered that the hypothalamus is a very small region "comprising in the cat, a cube the dimension of which is approximately four millimeters", (Ranson and Magoun—1939), and that according to Heslop (1938a) "even using the extremely weak current previously described, the histological changes are found to extend over an area of about three millimeters spherically from the point of the electrode." The motor responses of the stomach and intestine and the greater flow and increased acidity of the gastric juice, following the stimulation, more anteriorly, in the supraoptic and preoptic areas, are furthermore, still points of dispute. They have not been reproducible by all workers, nor is the cause or relationship between stimulation and response certain. It is not justifiable, therefore, to assume without question, that a parasympathetic center is being stimulated, although this may appear likely. It may be that cortical inhibitory fibres to the sympathetic center in the hypothalamus are being activated by stimulation. Such a possibility has been considered by Ranson and Magoun (1939) and by the work of the above authors in relation to the experiments of Kabat, Magoun and Ranson (1935), Kabat (1936) and Rioch and Brenner (1938).

After having dwelt for some time upon the motor disturbances in the gastrointestinal tract associated with lesions in the hypothalamus, we will depart upon a discussion of hypothalamic lesions in relation to gastrointestinal hemorrhage and erosions. Before doing so however, it is essential that we dwell for some time upon the anatomy of this region as illustrated in Fig. 3a. The diagram under discussion is an adaptation of an illustration from a paper by Beattie. It divides the hypothalamic region into three main portions, the supraoptic, the infundibular, and finally the mammillary. The experimentalists who have done the work as outlined in the foregoing pages as well as those whose work we will discuss under the heading of gastrointestinal hemorrhages and erosions, were well aware of the

great importance of the anatomical structures connected with the above divisions in the diagram. In front of the supraoptic region as shown in the figure there is located the anterior commissure. The reader will automatically visualize the supraoptic region when he is told that it is located above and somewhat in front of the optic chiasm. We are however, not so much interested in elaborating upon the supraoptic region because that has already been done not only by Sheehan (1940) but the neurologic and endocrinologic literature is full of material dealing with this region. The anterior commissure forms the anterior boundary of this basal region that is so very important in the physiology of interhemispheric func-



Schematic Drawing of Hypothalamic Region (after Beattie)

modified by us to illustrate the extent of the major stations of the Cerebral Basilar Autonomic Radiation
A-"anterior hypothalamic region" (preoptic)
B-"Tuberal (infundibular) area"
C-"posterior hypothalamic region" (mammillary)
D- anterior nucleus of thalamus
E- olfactoviscural nucleus of thalamus

Fig. 3a

tioning. In our later neuroanatomical discussions we will cite the extensive literature dealing with this structure. Here, it is sufficient to state that this commissure is almost as important as the posterior commissure. It extends from one hemisphere into the other and, as will be shown in later reference, it stretches beyond the thalamus of each side as well as beyond each internal capsule, being considered by some anatomists to be connected with parts of the corpus striatum. Therefore, it might be construed to be connected with not only vegetative function but also to possess functions of motion, tonus and to be responsible for variations in motor activities of the pyramidal and extrapyramidal types. The above qualities seem rightly assigned since, just as the thalamus is considered a modifier

of sensation, so the basal ganglia are modifiers of motion of the somatic and possibly vegetative types.

In the diagram of Beattie above there is also the infundibular region. It is superfluous for us to dwell upon the anatomy of this region since it has been adequately covered in the literature. Suffice it to say, however, that this region is intimately connected with the supraoptic in front of it and with the mammillary behind it. The last mentioned structure deserves some of our comment. The mammillary region of Goldstein (1906) and Holmgren (1920) [Beattie (1932)] is an extensive one being superimposed upon the infundibulum in front and stretching posteriorly into the mesencephalon. We are somewhat surprised that the author of the diagram did not include in it the interpeduncular area of Cajal. He did very well however to include in it the supramammillary commissure the function of which is the control of body size. This commissure connects not only the hypothalamus of each side but, because of the extensive ramifying properties of the last mentioned structures, the commissure may be conceived as connecting very important ganglia of both cerebral hemispheres. From the above brief reference to anatomy it becomes evident that the gastrointestinal functions as governed by the anatomical structures as illustrated in previous pages, cannot be said to be limited only to the region illustrated in the diagram of Beattie. The diagram therefore forms only part of the basal region with which our paper is chiefly concerned and which consists of both a telencephalic as well as a diencephalic portion (Figs. 1, 2, 3, and 4). This basal region is moreover very important to neuroanatomists and clinical neurologists because very little has been accomplished with it particularly in neurology, as far as syndromes of clinical value are concerned. That this area of the brain is involved in not only cases with convulsions but in many other types of brain disease is common knowledge. The syndrome of Wernicke proves it.

Although we were tempted to elaborate in more detail upon the anatomy of this area, particularly its septal, prethalamic, mesothalamic and its postthalamic region, and the connection of the above regions with the epithalamus and pineal we nevertheless must turn to the subject of gastric hemorrhage and erosion as dealt with by Sheehan (1940).

In his paper Sheehan first referred to the reports in the last decade of Mogilnitzky (1925), Korst (1928), Cushing (1932b) and then proceeded to the work of Durante (1916), Keller (1936b), Mann (1916), Stewart and Rogoff (1929), Kepich (1921), Stahnke (1924), Schiff (1867), Ebstein (1874), Brown-Sequard (1876), and finally that of Pomorski (1892). In discussing the experiments of the above authors and of those to follow we will touch merely upon the most important features of this problem of hemorrhage and erosion. The first experimental work on the subject of gastric hemorrhage and erosions as produced by lesions in the central nervous system was carried out by Schiff in 1867. This experimenter noted that an intracrainial lesion in dogs and rabbits involving the optic thalamus and adjacent cerebral peduncles would often lead, after a few days, to softening of the stomach and occasionally to actual perforations.

Schiff (1867), furthermore, observed similar changes following unilateral division of the pons, medulla, and spinal cord. From the above we can see where the actual pioneer work started. His experiments mentioned above therefore antedated those of Bechterev, and of Pavlov and stimulated the latter to look into the various other portions of the cerebral hemispheres. In those days looking for centers that might produce ulcers of the stomach is comparable to the present tendency to look for centers of convulsions, of consciousness, of sleep, of temperature control, of emotional regulation, of water, sugar and protein metabolism, etc., etc. Whether it is actual centers or merely ganglionated tracts that control the above and similar such functions is worth investigating.

These experimental observations of Schiff (1867) associating ulcerations with experimental injury to various parts of the brain were confirmed and extended by Ebstein (1874), Brown-Sequard (1867) and Pomorski (1892). The first experimental work on the diencephalon with this problem in mind was carried out by Burdenko and Mogilnitzky (1826). They used a subtemporal approach and made lesions of the brain immediately behind the infundibular stalk in a large series of animals (58 dogs). At this point we must stress the fact that gastrointestinal ulcerations should not merely be considered as trophic changes that follow nerve degeneration. That the process is centrally physiologic is shown by the fact that brain lesions produce changes in water metabolism when almost the same localities of the diencephalon are stimulated as those which produce ulcers.

To acquaint the reader with the work that followed the pioneer data as given above, we will merely mention the titles of the papers and some of the relevant facts. Dealing with the subject of gastric hemorrhagic erosions Oberling and Kallo (1929), did twenty-nine experiments in which lesions were made in the brain stem and diencephalon. Similar experiments were carried out by Hirata (1939) and those showed that tuberal lesions frequently gave rise to gastric hemorrhage and erosions. After Cushing worked on the injection of pituitrin and pilocarpine into the lateral ventricle of man, Light and Kendall (1932) produced gastric erosions in 94 per cent of their animals in whom pilocarpine was injected into the lateral ventricle. Underhill and Freiheit (1928) produced similar conditions by injecting pilocarpine subcutaneously.

Here again, we must state that just as it is important to associate convulsive phenomena with both sympathetic and parasympathetic activities on a biochemical plane, so in gastrointestinal studies comparisons between the brain centers governing either one of the last two mentioned types of function must be brought into play. The fact that pilocarpine produced specific gastrointestinal responses means that the diencephalon was stimulated. We will see these sympathetic and parasympathetic reaction types in our discussions of the subject of gastrointestinal hemorrhage and erosions. We will furthermore see these two factors of sympathin and parasympathin and the innumerable chemicals that fall into the category of one or the other and the related metabolic substances in the reports dealing with

brain lesions in relation to water metabolism. In the meantime it is noteworthy to mention the work of Keller, Hare, D'Amour (1933), of Watts and Fulton (1935) and that of Hoff and Sheehan (1935) along the above gastrointestinal lines.

Although in his technical discussion Sheehan (1940) presented a great deal of data dealing with instrumentation, and particularly with the Horsley-Clarke stereotaxie instrument for placing discrete lesions and mentioned the work of Martin and Schnedorff (1938), Keller (1906a and b), Watts and Fulton (1935), Hoff and Sheehan (1935), Burdenko and Mogilnitzky (1926), and finally Tenner and Bernheim (1939a and b), we will nevertheless dismiss the above data and present the essential features and scope of the experiments of one of these workers in the following quoted remarks (Sheehan p. 606): "Keller (1936a and b) in his recent publication on this subject has given data on 98 dogs in which hypothalamic lesions were performed in various parts (32 chiasmal, 20 partial hypothalamic, 30 massive hypothalamic, and 15 involving both the thalamus and hypothalamus). Of these 98 animals, 19 show gastrointestinal hemorrhage, and 8 multiple erosions. In an analysis of the anatomical localization of the hypothalamic lesions which led to gastrointestinal changes, Keller noted that of the 19 animals with hemorrhage 14 showed involvement of the supraoptic region, 3 encroached on the tuberal area, and 2 were obliquely cut; but in no case was the posterior (mammillary area of the hypothalamus) involved. In all but one the injury extended into the third ventricle." In addition to the above a controlled series of 101 dogs presenting 6 prechiasmal, 35 midbrain, 35 pontine and medullary and finally 25 cerebellar lesions are mentioned without specific tracts.

The material on the subject of hypothalamic production of gastric hemorrhage and erosions may be summarized in the following: 1) hypothalamic injury is followed by mucosal hemorrhage and erosions in about 1/3 of all experiments. 2) the site of the hypothalamic injury involves the tuberal and to a lesser extent the supraoptic region? 3) the large destructive injuries in the interbrain appear to be most likely to precipitate intestinal hemorrhage and erosions. 4) the relationship of such gastrointestinal changes to peptic ulceration is still obscure.

It must be emphasized that the neuroanatomy of this subject is still so confused that one is uncertain as to whether brain tumors produce vomiting and other symptoms referring to the gastrointestinal tract because of either focal irritation or the effects of general increase in intracranial pressure. This is seen in Sheehan's reply to Van Wagenen. This uncertainty is furthermore reflected in the question of the relation between sympathetic and parasympathetic irritation or depression. This is seen in Sheehan's reply to Bronk. It is relevant to note that this region of the diencephalon has been shown to be involved in patients suffering from convulsions associated with cerebral and cerebellar disease.

It seems safe to assume that not only ganglia of the cerebrum but various fibre tracts, pathways, radiations, commissure etc. not only of the hemispheres but also of the mesencephalon and lower structures are responsible for the gastrointestinal lesions that were produced as a result of stimulating or destroying parts

of the hypothalamus. It has been seen that the same can also be duplicated peripherally by bilateral adrenalectomy and other procedures affecting the sympathetic and parasympathetic system.

It has previously been emphasized that water metabolism is related to epilepsy because dryness of the mouth, sweating and urination occur as aurae before a fit, during a paroxysm, or after a fit. Just as gastrointestinal symptoms occur in relation to convulsive attacks or between the same, so do disturbances in water metabolism and micturition phenomena. Both of these systems are therefore neuroanatomically interrelated and each is in turn related to epilepsy. This subject will be dealt with in relation to neurogenic control by the hypothalamus and other portions of the diencephalon in the next few pages in a somewhat more detailed analysis of the literature. Later the same subject will be covered by the work of Watts, Frazier, and Uhle in connection with cortical experiments.

Before approaching the subject of water metabolism it might be well for us to concentrate upon some anatomically related facts. Although the anatomy of diencephalon is incomplete, the subject of the cellular structure of vegetative centers of the cerebrum in general has received attention. Some outstanding names are mentioned in connection with the anatomical studies of these portions of the brain. The names of Greving, Malone, and Morgan will be amply dealt with in the review of the literature of the neuroanatomy to follow. Associated with the names of the above investigators will be the extensive works of Muskens who concentrated largely upon the connections between the corpus striatum and the medial longitudinal fasciculus. In the course of study this great investigator of the subject of epilepsy spent most of his time between the physiological laboratory and the department of anatomy. He finally developed the details of the connections between the fasciculus mentioned above and the posterior commissure. In doing this he made possible the establishment of the fascicular tract which ends by the side of the lateral horns of the spinal cord below and connects with the vegetative structures in the posterior hypothalamic area. The spinal cord area may be that of Bok.

Another investigator who was also primarily interested in epilepsy and who is more famous for his anatomical studies, particularly those connected with the intercortical system, is Joshua Rosett (1939). The monumental work of Rosett on the intercortical systems will be dealt with particularly in its relationship to the vegetative nervous system because of the connection between the anterior thalamic neurone fibres, going to the cerebral cortex, with his elaborated cingulate gyrus system. This connection of the cingulate with the long association systems will be a very important subject when we attempt to present the anatomical basis of the work of Watts on the control of the gastrointestinal system by the cerebral cortex. Although most of the work of Rosett dealt with the cerebral cortex, some of it, particularly the physiology, was concerned with the diencephalon. Not only will the work of Rosett, and that of Campbell, Mills, etc., concern us in relation to the above gastrointestinal studies, but it will also serve to link autonomic functions such as pupillary changes during a fit, eye movement, head and neck move-

ment and other features of the pattern of attack that were completely developed in the work of Foerster, Vogt, Penfield and associates with the physiology of specific corticodiencephalic tracts. Just as Muskens developed his anatomical studies as given above so that his view on myoclonic reflexes might have a basis, so did Rosett spend a great part of his life on the neuroanatomy of the cortex in order that he might be able to understand autonomic and other manifestations of epileptic attacks; the latter being one of his chief interests.

One might even condone Rosett for his transgression with regard to the structure of his figure on page 41 of his book on the basis that he was anxious to simplify all brain tracts and radiations and in doing so he omitted certain necessary portions of the vegetative nervous system. A careful look at his diagram also discloses that he attempted to unify the motor, sensory and vegetative structures so that they might be connected with his intercortical system. It is also possible, but not probable, that Rosett (1939) was attempting to impress us with the fact that topographically speaking the central nervous system might be considered as a longitudinoaxial bicellular or a bidimensional and tridimensional tricellular structure. We know for instance that he was very familiar with the details involved in the fine mechanism of the area giganto pyramidalis. In the human being this structure consists of about 80,000 large cells, the largest in the body perhaps. In the adult monkey this same structure consists of about between 20,000 to 30,000 cells. This structure furthermore forms part of the final pathway. In looking through Rosett's book (1939) one can see that he was very familiar with bioelectric phenomena in relation to the central nervous system. His repeated citations of Adrian and others lead one to believe that he might have had in mind a simplification of electrical, anatomical and chemical phenomena to suit his efforts. This attempt at simplification interests neurophysiologists. It might also explain the fact that certain areas in the motor and premotor cortex contain the functions of movements of skeletal and also that of intestinal musculature. We have however no desire at present to speculate on what might have been in Rosett's mind. He did do one specific important thing in the above connection. He showed that the telencephalon works together with the diencephalon as one unit to control vegetative functions.

Although one can overlook some anatomical shortcomings in an individual who is primarily an outstanding anatomist, one finds it difficult however to overlook Rosett's attempt at anatomic simplification of the diencephalon. He did however emphasize the functions of the autonomic nervous system in relation to gastrointestinal and metabolic action when he attempted to include chemical features in relating sympathin to parasympathin.

In his presentation of Myerson's diagram, Rosett discusses fear and pain in relation to the function of the sympathetic and parasympathetic systems. Under the former he lists adrenalin and benzedrine as having an adrenergic action. He also shows that acetylcholine is produced at the synaptic junction. At a similar point of the diagram he shows anatomically where sympathin is produced. Under this

heading of sympathetic action he emphasizes that atropine blocks the action of acetylcholine or mecholyl. The above discussion of the action of the sympathetic system is a very important one. One constantly meets with such problems in epilepsy. A great many substances related to the phenol ring such as tyrosine, thyroxin, a large part of the endocrine group of substances, the above including not only adrenal cortex hormones but also testosterone, and various others may be listed under the heading of substances chemically related to adrenalin. Upon the action of such substances depends not only the chloride, sugar, but also water metabolism. Before proceeding with water metabolism a knowledge of both the anatomical and chemical implications of diencephalic function are essential. Under the heading of carbohydrate metabolism comes a great list of compounds ending in the final common compound of pyruvic acid. The phenol group which we noted in sympathin also seems to enter into the cycle of pyruvic acid as seen in the reports of phenyl pyruvic amentia by Gibbs and Gibbs. These authors find that feeble minded persons who have a disorder of protein metabolism with excretion of phenyl pyruvic acid in the urine have electroencephalographs which show many fast waves of abnormally high voltage and many abnormal slow waves. We can see how the pioneers on the diencephalon, while working with pituitrin and pilocarpine, opened a field of bioelectric chemistry. From the above we therefore see that the transmission of the nerve impulse is related not only directly to adrenalin but also to other chemical substances of the protein carbohydrate and other groups.

The structure of the sympathetic and parasympathetic system in relation to somatic fibres within the brain tracts is therefore important not only from the viewpoint of their relation to variations in impulse transmission rate such as seen in the A.B.C. fibre types but also to the form and voltage of brain waves. The familiar work of Kornmuller in the relation of the latter to the region of the diencephalon has been shown. It has also been proven by Kreezer (1937a) and Kreezer (1936) that there is a significant correlation between intelligence and the alpha index (per cent of time that alpha waves are present). The relation of the pyruvic acid group to carbohydrate metabolism has been further shown by Fearon. The substance mentioned above forming a chain reaction with lactic acid, and the fact that the pyruvic acid can undergo union with itself and form a five carbon aliphatic acid and finally, the structural connections of these with phosphorus and nitrogen are very important. Also important is that its relationship to fatty acid metabolism and to glycerose have been established. One therefore cannot overemphasize the bioelectric and biochemical linkage in all types of metabolism, especially to the water metabolism concerning which we will present literature.

The relation of the above compounds to water in the body and to the carbon and phosphorus compounds in the body is emphasized by the same author Fearon. The association of cholesterol to the reticuloendothelial system is emphasized by Cantarow and Trumper (1932) and the fact that the gastrointestinal tract because of the liver becomes chemically related to sympathetic and parasympathetic

systems is also discussed. Here we finally see the relation of all the preceeding to gastroenterologic neurophysiology.

Just as Rosett's data on the action of sympathin can be elaborated and connected with not only nerve transmission in their autonomic and somatic nerve fibres, but also to all forms of metabolism including that of water, so can the data presented dealing with the parasympathin group. Pilocarpine and pituitrin belong to this group. These substances are important, not only in gastrointestinal function but the mechanism of the convulsion is related to both of these systems. This has previously been shown in the fact that a convulsion can be observed in substances which contract the pupils such as creatinin (Furstner) and pictroxin (Pollack) as well as in substances which dilate the pupil such as absinthe. Cushing was the first to stress the parasympathin effect.

Rosett's statement dealing with the parasympathetic is also of importance. Before leaving this subject and going to water metabolism some remarks on the parasympathetics seem essential. Under that heading Rosett lists physostigmin or prostigmin as destroying esterase and as enhancing the response to acetylcholine or mecholyl. He furthermore shows where esterase is present and checks the action of acetylcholine. We present the following quotation from Fearon which summarizes the above relationship. "Sympathin is liberated locally on stimulation of the sympathetic nerve. Parasympathin is a dialysate acid stable substance destroyed by alkalis and esterases, present both in the blood and in tissues. The manner in which a neurocrine such as the above operates is uncertain. Presumably it is set free by an activation or change in valency electrons in the parent substance as the result of the arrival of a nerve impulse. The liberated neurocrine then reacts with some tissue constituent and starts the series of chemical changes involved in muscle contraction or gland secretion." Here we find the autonomic and somatic symptoms being related to all forms of metabolism.

Water metabolism was first related to intestinal absorption by the work of Klisiecki, Verney, Pickford and Rothschild (1932). The relationship between the action of the pituitary gland and water diuresis was proved by Theobald and Verney (1935) and finally supported by the work of Haterius (1939). The antidiuretic action of acetylcholine and the relation of the liberation of a pressor substance by the pituitary through the action of the hypothalamus has been shown by Chang, Chia, Hsu, and Lin (1937), also by Dikshit (1935) and finally by Pickford (1939). Before the above work was started, Verney (1926) showed that the pituitary was related to renal secretion. Painful stimuli and the injection of a posterior pituitary extract were shown related to water metabolism. Exercise and emotional stress were also shown to be connected with diuresis. The former by Norris and Weiser, and the latter by Rydin and Verney (1938). One will readily see why we stressed the anatomy and physiology of the diencephalon by referring to the structures in Fig. 4.

Richter (1938) fed thyroid to animals and noticed the increase in water consumption with the accelerated metabolism. White, Heinbecker, and Robinson

(1938) disagreed with the previous report. They, as well as Mahoney and Sheehan (1935), showed that thyroidectomy during polyuria and polydipsia restored water exchange to normal. At this point we can realize that our elaboration of sympathin and adrenalin producing structures to thyroxin, the latter being a diiodo-tyrosine, has not been overemphasized. It seems that one chemical chain directs not only other forms of chemical process in metabolism but has a particular influence upon water exchange as seen in polydipsia and polyuria experiments. The above functions as well as the chemistry are of course related to the various portions of the hypothalamus the anatomy of which we have elaborated upon. The relation of cutting the pituitary stalk to the specific gravity of the urine has been shown by Fisher, Magoun, and Hetherington, also by White and Heinbecker as well as Ingram, Ladd, and Benbow, while Bellows and Van Wagenen claimed

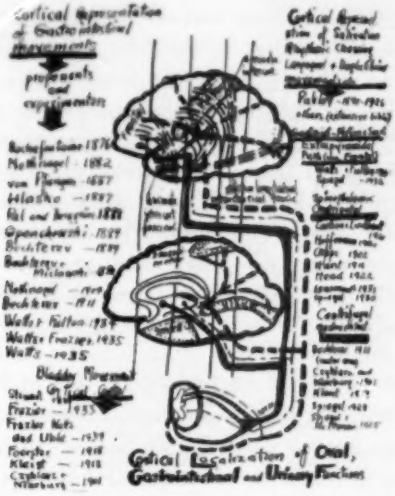


Fig. 4

that diabetes insipidus is essentially a water retention disease. Richter (1935) produced hypothalamic lesions and noted that in such cases polydipsia followed the polyuria. Other interesting items mentioned by Hare (1940) was the relation of intravenous sodium chloride to thirst as shown by Gilman (1937). The last mentioned investigator also noted that a similar administration of isomolar urea did not produce dryness of the mouth. In the relation of the chloride metabolism to that of water we must again realize that chemical substances related to adrenalin and sympathin also play a part in such metabolism. Indirectly, therefore, there is a relationship because of neural regulation by the autonomic between the endocrine system and nerve centers controlling water metabolism.

In his presentation of the literature of the subject of water metabolism, Hare (1940) shows that diabetes insipidus can be produced by destruction of the

supraopticohypophyseal system. That destruction of such can be accomplished by genetic factors is shown by Gee (1877), Weil (1884), Clay (1889), and Gaupp. Neoplasms were shown to produce the same effect upon the above structures by Stringer (1933). From the above we see that the subject of water metabolism in relation to the diencephalon has a solid foundation in clinical as well as in laboratory findings which were begun in the middle of the last century. Before connecting the data which we have presented with the material to follow, we should like to mention that Hare (1940) emphasizes the physiologic mechanism concerned with the control of water diuresis. He claims that ingestion of water in relation to thirst is not understood. He cites experiments relating thirst to the section of olfactory and trigeminal nerves (Bellows and Van Wagenen-1939). Hare makes the distinction between thirst and dryness of the mouth in relation to salivary gland action as shown in the work of Steggerda (1939). This symptom complex is met with not only in epilepsy but also in many diseases associated with diencephalic, telencephalic, and brain stem lesions.

In the above, on the physiology of water diuresis, Hare mentioned the work of Darrow and Yannet on extracellular electrolytes. He also discusses the work of Adolph in relation to the feeling of satisfaction of the thirst and the time water reaches the tissues. Among the above he mentions the work of Dill and in the actual physiologic experiments he mentions the work of Fisher, Ingram, Ranson, as well as that of Fisher, Magoun and Hetherington. He furthermore discusses the mechanism concerned with daily water ingestion as worked out by Richter (1938) and water in relation to body weight as established by Gilder and Phillips. Hare then proceeds to discuss the work of Burgess, Harvey and Marshall on the relation of function of the posterior lobe of the pituitary to renal tubular absorption. He cites the work of White and Monaghan, that of Shannon, and that of Van Slyke and his collaborators on glomerular filtration.

Hare goes into rather great detail on Shannon's (1936) work dealing with the water concentration in the urine as compared with that of the plasma. It is important to emphasize here and now that at no time will it be superfluous to elaborate upon the exact diencephalic anatomical connections. References to the anatomical literature of structures that regulate such vital functions are never enough particularly if there is disagreement among neuroanatomists with regard to not only cellular structure but also with regard to the origin and destination of fibre tracts leading to the cellular masses of the diencephalon. After giving the material on renal bloodflow as developed by Van Slyke, Rhoads, Hiller and Alding (1934), Hare covers the subject of tubular absorption of water, chloride, urea, and glucose as worked out by Shannon and Fisher (1938). Finally after citing the work of Walker (1939) on the improved methods of separating antidiuretic principles from other substances, he gives an account of the chemical method of isolation and identification of antidiuretic substances from body fluids as worked out by Newton and Smirk (1934) and by Tsai (1939).

The reason for the attraction by the pioneers to the field of the hypothalamus in relation to the stomach and intestines as well as the hypothalamus in relation to water metabolism may be seen from the following. The hypothalamic region is located in a sector of the brain which is very conducive to the formation of neurological syndromes. In many of our cases of epilepsy (Fitch, Pigott and Weingrow, 1938-1942) we have given proof that rather extensive involvement of this region exists. This basal sector, Fig. 1, forms the body of the anatomical basket to which we have previously referred. When one views the horizontal sections through the brain as seen in Tilney and Riley (1923) it may be noted that fibres originating in the hypothalamic regions fan out in all directions so that they can reach not only the frontal, the temporal, the occipital, and the brain stem but also communicate with the other cerebral hemispheres. At the levels mentioned above

Fig. 5

through the hypothalamus at the level of the internal capsule and through the mammillary region at the level of the mesencephalon, there seems to be no obstruction by ventricular formations when compared with the other horizontal sections through the brain and in the figures on pages 920 and 914 of Tilney and Riley.

For the above and many other reasons the great investigators in the past such as Brown-Sequard, Gee, and others as well as the modern workers to be presented herewith experimented not only with the subjects under consideration but also with this region as a center for tonus and even convulsive phenomena. Those mentioned by Hare as continuing with the experiments include: exercise (Norris and Piser) emotional stress (Rydin and Verney-1938). The work on the thyroid in relation to water consumption was done by Richter (1938), and disagreed with by White, Heinbecker, and Robinson (1938), as having a definite relationship.

Although the work on other endocrine glands could be mentioned in this connection none seem as related to the general metabolism as the thyroid. In regard to the subject of the thyroid in the above connection as far as polydipsia is concerned, the names of Mahoney and Sheehan (1935) as well as White, Heinbecker and Robinson (1938), should be stressed.

The names of Richter, Fisher, Magoun, and Hetherington, White and Heinbecker, Ingram and Ladd as well as Bellows and Van Wagenen, in connection with adrenal water, water deprivation and specific gravity of urine, as well as water retention in relation to diabetes insipidus may be listed with the names of Fisher, Ingram and Ranson as well as those of Fisher, Magoun, and Hetherington who worked on the question whether polyuria precedes polydipsia. Although patients suffering from convulsions present brain lesions that produce diabetes insipidus it is remarkable that epileptologists have thus far failed to elaborate upon this problem. They have elaborated more than enough on the relation of epilepsy to diabetes mellitus and hypoglycemia, etc. Hence our emphasis on the important features of water diuresis, etc. Although the attention of all of these workers to the basal structures of the cerebral hemispheres was on the basis of physiology, most of the material which the experienced neurologists present has a very intense anatomical coloring.

The subject of water metabolism has other angles so that it may even be connected with the problem of temperature control. In this work we limit ourselves to those subjects in water metabolism which are connected with those brain centers either in the hypothalamus or cortex that control micturition and related functions. Even though Hare deals with water metabolism from the viewpoint of its neurogenic factors, here and there he touches upon mechanical factors as seen in his references to Dill, Adolph, Richter, and to the work of Darrow and Yannetl, on dryness of the mouth in relation to extracellular electrolytes.

When the analysis of Hare is compared with that of Sheehan on the gastrointestinal tract one finds that the former is rather short of references to neuroanatomy. This shortcoming is however excused because the subject is covered in the papers on experimental diabetes insipidus by Ranson, Fisher, Ingram and Magoun, Ranson, Balado to which Hare gives detailed references. The anatomy of the diencephalon not only from these angles but from the view of an epileptogenous center is important. In spite of the work of Bravais and Jackson, most authorities point to the diencephalon as the seat of origin of the unilateral and generalized fit, particularly of its tonic component.

From the previous analysis of the literature on gastrointestinal tract control as well as that on the regulation of water metabolism by the basis cerebri, we can very well conclude that the parts of the brain under consideration have been anatomically looked upon as a region that holds a great deal of promise not only with respect to visceral function but also as a spot in which a great many neurological syndromes can be expected to be located by the workers of the future. No one can deny that workers such as Schiff, Brown-Sequard, Horsley, Sherrington,

etc., would feel that the centers of the functions under consideration would be limited to this region alone and are not to be connected with crucial structures higher up in the region of the thalamus (diencephalic basal ganglion), the globus pallidus, the putamen, as well as the cerebral cortex of the frontal, temporal, occipital, and the cortical structures between, in front of, and on both sides of, the optic, tuber, and mammillary regions. The reader is therefore urged to familiarize himself further with the anatomical elaboration of this region as seen in literature on diabetes insipidus up to the year 1928 as presented by Fink (1928). He can furthermore supplement his physiological knowledge on the subject of water metabolism by referring to diabetes insipidus as produced by lesions in the supraopticohypophyseal region as shown in the work of Bailey and Bremer (1921), Dott (1922), Gurgus (1924), Reichert and Dandy (1936), Ingram and Fisher (1936), Magoun and Fisher (1939), Biggart and Alexander (1939), and various other workers who deal with the subject of mechanical factors.

It might seem to the reader that we have in the previous pages been unusually repetitious in regard to the subject of neuroanatomy of the vegetative nervous system within the cerebral hemispheres that control gastrointestinal function as well as micturition. This will be justified in our analysis of the literature on neuroanatomy which we will present in further pages. It will be shown for instance, that the neurological clinician often finds it difficult to point to definite tracts that are concerned with autonomic function not only in the regions under consideration but also in the brain stem and spinal cord. All the literature seems to be confused with regard to specifically locating autonomic function so that even in spinal diseases, the clinician is perplexed as to whether to place certain clinical phenomena in the pyramidal tract, in the lateral and anterior spinothalamic, in the rubrospinal, in the tectospinal, in the lateral ground bundle or other tracts especially the olivospinal and tectospinal. All of these tracts have been looked upon with suspicion; and although clinical proof has been produced that some of these contain autonomic fibres, the writers of textbooks have refrained from committing themselves. We are therefore faced with this problem in considering localization of gastrointestinal and metabolic functions. It is our feeling that such hesitancy should be once and for all cleared and that the clinical evidence for autonomic function not only within the spinal cord but also within the cerebrum should be definitely established. This can be done only when one takes all data whether clinical, experimental, or anatomical into consideration. The tracing of such tracts into the diencephalon and particularly into the hypothalamus will be the duty of the neuroanatomist once sufficient clinical and experimental material has been organized. Hence one should not neglect to pay attention to the work of the modern investigators on infection in relation to the hypophysis by Hall (1923), McGavack and Benjamin. The studies of polydipsia in dogs have been carried out by Mathews (1915), Dott (1922), Curtis (1924), Mahoney and Sheehan (1935), Warner (1931), Reichert and Dandy (1936), Bailey and Bremer (1921), Bellows

and Van Wagenen (1937), and Biggart and Alexander (1939) and by Magoun, Fisher and Ranson (1939).

It is needless to emphasize that the workers mentioned above followed along the lines of not only the work of Schiff, and other pioneers on the autonomic nervous system but particularly upon the special papers dealing with water metabolism as first published by Gee (1927), Weil (1884), and Clay (1889). Further references to this subject may be found in the bibliography. It is beyond the scope of this paper to give detailed accounts of the work done by each investigator on this subject. Those who are interested in the anatomy of the autonomic above the mesencephalon should not neglect to refer to these workers since therein one will find not only data on water metabolism, material on vegetative centers connected with gastrointestinal function, micturition, but also other related subjects of clinical importance. We can point however to a number of such experimentalists and neuroanatomists whom Hare mentions particularly. Those who experimented on polydipsia in rats, such as Dodds, Noble, and Williams (1937), Gilder and Phillips, Richter (1935), Sandbury, Perla and Holly (1937) and White (1937) are cited. The same subject was studied in chickens by Laccassagne and Nyka (1935), and in cats by Dodds, Noble, and Williams (1937), Farr, Hare, and Phillips (1938), and by Ingram and Fisher (1936).

Before proceeding with the subjects of gastrointestinal control by the cerebral cortex and the function of micturition as governed by the cortex of the various cerebral lobes, it is important that we impress the reader with the fact that the subject material of our paper deals not only with such systemic functions but also the mechanism of the convulsive state. The paucity of material in the literature on epilepsy forced us however to digress to nonconvulsive subjects. The above physiologic data leaves one clear neuroanatomic problem in our minds. Are gastrointestinal and water metabolism regulations carried mainly by diencephalic and tectal structures? When vomiting or urination occurs in connection with a cerebellar lesion is it because of cerebellotectal fibre stimulation? Where vomiting is present in vestibular syndromes is it also due to connection with tegmental visceral tracts? It is not unlikely that the brain section experiments though covering various structures merely point to one pathway which has various ramifications. In other words cerebellar tumors do not press on "vital centers" and cause vomiting but connect with them! We will now leave the subject of the diencephalon hoping that the reader has been impressed with its importance and proceed to the centers governing gastrointestinal functions above this structure.

(*To be continued*)

FISSURE-IN-ANO*†

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Fissure-in-ano is a common and usually painful proctologic disorder occurring about equally in both sexes and with its highest incidence in the third and fourth decades. As generally understood, it refers to a simple ulcerative lesion usually in the posterior anal commissure; less commonly it is situated anteriorly, 8 per cent in females and 1 per cent in males. The anterior fissure is usually less extensive and has a milder symptomatology. The typical anal fissure involves the posterior anoderm overlying the subcutaneous portion of the subcutaneous external sphincter muscle. Ulcerations which occur higher in the anal canal overlying the puborectalis portion of the levator ani are sometimes referred to as "high-lying" fissures which are apt to produce a great degree of levator spasm with referred orthopedic, neurologic or gastrointestinal symptoms. Their etiologic basis is different from the common anal fissure and they require a special therapy. Anal fissures comprise about 6 per cent of proctologic conditions of infancy and childhood. They usually occur secondary to gastrointestinal disorders with irritating fecal discharges.

Pathogenesis and Anatomic Considerations

A variety of conflicting explanations have been advanced regarding the etiology of fissure and its common posterior location. Repeatedly cited are the passage of hard stool which ruptures the delicate anoderm posteriorly, tearing down of an anal crypt with erosion, infection of a duct or preformed anal gland, "cryptitis", submucosal hemorrhage, etc. Why these conditions should so regularly occur in the posterior commissure and so infrequently before the third and fourth decades has never been satisfactorily explained. Many authors attribute a lack of support in the posterior commissure to the fact that the subcutaneous fibres of the external sphincter muscle swing across the crotch of the diverging *superficial* fibres of the external sphincter leaving an area described as "the weakest part of the whole anal ring", hence the posterior location of fissure. They further describe the subcutaneous portion of the external sphincter as being "relatively weak and unsupported". The true explanation for the almost constant location of the fissure in the posterior commissure may depend on several factors, but we consider the following to be the most important: the first is the anatomic which has always been overstressed; the other is the pathologic which has been understressed.

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Anatomically the abrupt axial change of the anal canal to the rectum forms the so-called anorectal shelf. In the act of defecation or active dilatation this posterior shelf flattens out and is subject to much greater tension than the anterior commissure where the anal and rectal linings continue in the same plane. This axial change predisposes the posterior anoderm to rupture.

Pathologically, the posterior commissure is also predisposed to fissure because fibrosis (pectenosis) with fixation of the anoderm is very commonly found in the fissure patient, and the fibrotic infiltration of the posterior anal tissues unquestionably is an important precursor to fissure. In fact, the mobility of the posterior shelf is greatly diminished and the fibrosis and fixation in some cases is so advanced that it produces an incapacitating anal stenosis. The rupture occurs posteriorly in fissure not because this is the weakest point of the anal ring, but because in dilatation of the anus, either mechanically or physiologically, the posterior anoderm either is, or becomes a fixed point.

Similarly, the chonic anterior fissures observed in the female commonly arise on the basis of a perineal tear where there has been scarring, infection and fixation of the anoderm.

Chronic fissures are actually anal ulcers and their failure to heal is primarily due to inadequate drainage with resultant persistent cellular saturation of the tissues, lymphedema, histaminia, induration and, finally, fibrosis (pectenosis) with fixation of the anoderm and intermuscular septum of the posterior anal arc. The ulcer is repeatedly traumatized, not necessarily by the passage of the stool, but by the mere muscular activities of the sphincters, and particularly of the levator ani, through its posterior insertion, and the fibro-elastic extensions of the conjoined longitudinal muscle. Adequate drainage with release and division of the musculature and eradication of the fissure bed with its fibrotic fixation is the essence of radical fissure surgery (Fig. 1).

Classification

The *acute* fissure is a recent linear erosion or rupture of the anoderm. Many of these heal spontaneously, but it should be noted that an underlying fibrosis with some fixation may already be present, and the basis for recurrence well advanced.

In the *subacute* fissure the erosion has penetrated to the anal fascia overlying the muscle, and definite ulceration with beginning induration of the anodermal edges and more fixation and fibrosis are present. Anal spasm is intermittent but prominent after defecation.

The *chronic* fissure is characterized by further progressive pathologic changes primarily following inadequate drainage with repeated infection, venous congestion, lymph stasis, local histaminia, and, not infrequently, submucous fistula. These pathologic processes usually produce the so-called "sentinel pile" externally, the enlarged papilla or epithelial polyp internally, and chronic interstitial fibrosis (pectenosis). This irreversible "pathologic triad" together with a chronic endo-

neuritis in the fissure bed and a status "spasticus analus", complete the picture of the chronic indurated fissure with its usual dyschesia and defecophobia.

Symptomatology

Dyschesia, varying greatly in character, intensity and duration, is the common complaint. In the interim between evacuations a sense of throbbing, soreness or irritation may be present. Intensity of the pain during evacuation depends on the degree of anal tension and dilation. The fissure patient, in anticipation of a painful defecation, is commonly addicted to catharsis, usually mineral oil. This is erroneously termed constipation. Many fissure patients, through catharsis, have secondary gastrointestinal symptoms.

Fig. 1—The pathology is excised in toto. The musculature is then incised as indicated.

Bleeding is less common, and in contrast to that associated with hemorrhoids is secondary or absent. In the chronic fissure it may be intermittent.

Pain or spontaneous purulent discharge from a postanal infection may be the initial symptom. Occasionally the "sentinel pile" may be interpreted as a hemorrhoid and invite medical advice.

Referred symptoms sometimes predominate and may be misleading. Reflex anal and levator spasm may produce pain in the lumbar region, coccydynia, pseudococcygitis, sciatica, dysmenorrhea, dysuria or urinary retention and rather acute abdominal pain. The chronic fissure patient may develop a prostatism with defecatory inhibition, a spurious diarrhea, and even a general neurosis.

The occasional fissure which involves the upper anal canal overlying the puborectalis muscle may produce severe levator, coccygeal or pyriformis spasm

with reflex symptoms. These are often misinterpreted and considered orthopedic or gynecologic symptoms rather than proctologic.

The so-called "spastic" type or high-strung patient with a distinct spasmophilic diathesis presents a real problem. In these patients in whom chronic spasticity of the anorectal musculature is etiologically significant to the fissure, there is usually present chronic constipation, flatulence, abdominal cramping and other manifestations of colonic dysfunction. These patients require careful consideration and study from a gastrointestinal and neurologic point of view. Several of these patients have been observed in whom surgery was followed by an intractable neurosis. Complete dilatation—not divulsion—of the anal musculature under deep anesthesia, or the use of the oil soluble anesthetics, should be tried before surgery, if operative interference appears advisable.

Diagnosis

The diagnosis is usually made by simple inspection. However, in their acute phase fissures may be missed, in which case the diagnosis made is usually hemorrhoids. The occasional high-lying fissure may require careful instrumental examination. The fissure patient is difficult to examine. The slightest tension by finger or instrument usually produces severe pain and muscular spasm which quite precludes a satisfactory examination. Painful and unsatisfactory maneuvers may discourage further proctologic investigation, and serious lesions such as carcinoma may be entirely overlooked with catastrophic results. Local topical anesthesia is usually useless. Unless contraindicated, 10 to 15 cc. of an oil soluble anesthetic (Anucaine, Fig. 2) or procaine should be injected into the posterior tissues. The resultant anesthesia permits a painless and complete exposure of the fissure and a comprehensive digital and proctosigmoidoscopic examination. The etiologic significance of associated pathology (hemorrhoids, papillitis, pectenosis, pelvic tumor, retroversion, rectocele, prostatitis, and possibly related gastrointestinal or neurologic conditions) requires proper evaluation. All of these conditions are pertinent to the selection of adequate therapy, particularly surgery. The common practice of anticipating a complete examination at the time of operation may unsuspectingly disclose a lesion requiring somewhat more extensive surgery than anticipated and for which both patient and surgeon are unprepared. In the examination of nervous individuals and children, preliminary sedation with the barbiturates or even morphine and atropine may be advisable.

Differential Diagnosis

Chancre, chancroid, epithelioma and colloid carcinoma are the most important conditions requiring careful differentiation. Chancre can be easily mistaken for simple anal fissure. Differential points are less pain, shorter history with possible sodomy, serous discharge, undermined edges, and perhaps palpable inguinal nodes. In suspected cases a dark field and serologic tests are indicated. Epithelioma (Fig. 3) and colloid carcinoma are characterized by chronicity, deep, rather firm, indurated, grayish margins with an indurated base. Inguinal adenopathy may be

already present. Biopsy is indicated. Marginal erosions secondary to anal tuberculosis, lymphopathia venereum, gonorrhea, or ordinary pyogenic infections are usually lateral. Early ulceration of agranulocytosis may be confusing.

Postoperative fissure resulting commonly from persistent muscular spasm, inadequate skin drainage, or placing the stumps of excised hemorrhoids too close to the commissures requires separate consideration since it is often highly refractory to ordinary therapeutic measures. A posterior sphincterotomy with adequate skin drainage may be necessary for ultimate healing. Recurrent fissures following fissurectomy or fissureotomy may be embarrassing. They result from failure to incise completely the subcutaneous external sphincter muscle or to remove adjacent hemorrhoids, hypertrophic papillae or redundant mucosa which interfere with adequate drainage and healing. Bridging in the fissure wound, infected sinus and persistent muscle spasm, particularly in the spasmophilic patient, are common causes of recurrence.

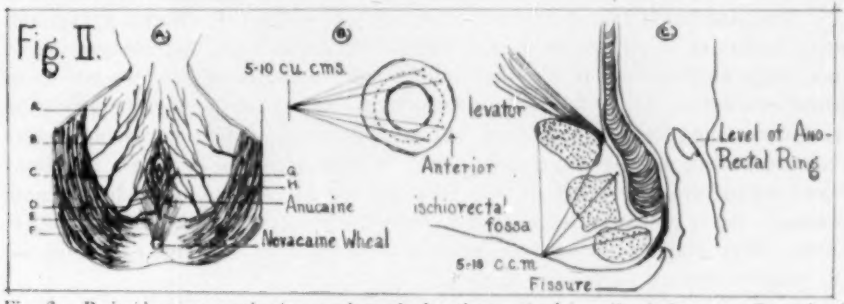

Fig. 2a—Perineal nerve supply (very schematic for clearness). A, small sciatic nerve; B, perineal branch of small sciatic nerve; C, perineal nerve; D, inferior hemorrhoidal nerve; E, branches of fourth sacral nerve; F, anococcygeal nerve; G, external sphincter muscle; H, gluteus maximus muscle.
b—Direction of the injection for fissure (According to Morgan).
c—Showing depth of injection for fissure.

Treatment

Successful treatment of fissure-in-ano requires proper evaluation of the entire pathology and pathogenesis. Careful examination with complete evaluation of the entire fissure pathology usually relegates the case into a surgical or nonsurgical group. In cases described as subacute, nonsurgical measures may be tried, but these are frequently disappointing. The criteria for chronic indurated fissure have been emphasized because palliative measures are useless. Many chronic and subacute fissure patients, through inadequate treatment, are deprived of the euphoristic benefits of a normal bowel evacuation through ill-advised injections, so-called "anesthetic ointments and suppositories", dilatations, and particularly continued harmful catharsis.

Nonsurgical Palliative Treatment

In the recent fissure, local applications of the so-called anesthetic and stimulating ointments or suppositories with gentle dilatation may relieve the pain

sufficiently to prevent sphincter spasm and permit further healing of the fissure. Defecatory trauma should be aided by appropriate catharsis, anal hygiene, hot Sitz baths, etc. The common practice of cauterizing the acute fissure with nitrate of silver, phenol, zinc chloride, etc., without adequate anesthesia is mentioned only to be condemned. It is extremely painful and provocative of severe muscle spasm with subsequent increased defecatory trauma. The failure of the anoderm to close in the recent fissure is primarily due to repeated trauma, painful muscle spasm and inadequate drainage.

A simple and effective method of relieving and often curing recent fissures is the injection of an oil soluble anesthetic, the use of which was devised and recommended by one of us in 1929 (Gorsch), and has been used extensively in one form or another since that time. We prefer the oil soluble anesthetic, Anucaine. The use of oil soluble anesthetics requires a special technic which must be carefully observed, and is described subsequently in detail.

Anucaine has been a boon to the acute fissure patient. It relieves spasm and pain, facilitates local treatment, and permits of a thorough and comprehensive proctologic examination. It abolishes painful reflexes and overcomes the terrors of bowel evacuation. Minor surgical procedures, when indicated, may frequently be done under the prolonged anesthetic effects of Anucaine. All the foregoing factors promote healing and in some cases result in permanent relief. These injections afford a long interval with relief from pain and sphincter spasm, provide adequate drainage, the opportunity for further healing and the correction of adverse bowel habits. They may be repeated at intervals of from 7 to 10 days, depending on the progress toward permanent healing.

The injection of an oil soluble anesthetic is followed by gentle dilatation, not divulsion, of the anal musculature. The subsequent use of topical applications such as ichthyol and scarlet red ointment on alternate days promotes healing. Fissures with sluggish, indolent bases are best treated with cautery or curette. During the healing period hard, painful evacuations should be avoided by the proper use of oil instillations or mild catharsis. (In cases of marked levator spasm or those with a high-lying fissure, the oil injections should be given through the puborectalis muscle.) Oil injections may be repeated several times, but fissures failing to respond usually require surgery for permanent relief.

Technic of Injection

The patient assumes the lateral Sims or inverted position. The ampules are previously warmed and aspirated into a 10 cc. Luer Lok syringe armed with a large-bore needle or canula. The canula is later replaced by a 4-inch Luer Lok needle of 19 or 20 gauge. The postanal skin is shaved, cleansed with alcohol, prepared with tincture of merthiolate and infiltrated with a small amount of novocaine. The larger needle with syringe attached is introduced through a small wheel 3 cm. posterior to the anal verge, or inserted well below the skin into the cellular tissues of the perianal skin on either side of the anal musculature. Five to 8 cc. of

Anucaine are distributed in the posterior quadrants. The oil may be injected directly into the anal sphincter guided by a finger in the anal canal after the tissues on either side of the sphincter have been injected (Morgan). A small amount of the oil may be injected directly under the fissure bed (Fig. 2). The anterior quadrants may be injected through laterally placed wheels if desired. The anesthetic oils should not be injected into the skin and should not be pooled in the tissues. Best results follow an even distribution around branches of the inferior hemorrhoidal, fourth sacral and posterior sacral nerves.

Surgical Treatment

Dilatation:—Dilatation, or stretching of the sphincter, now largely outmoded, was at one time a favorite method of treating fissures. It is not a simple procedure.

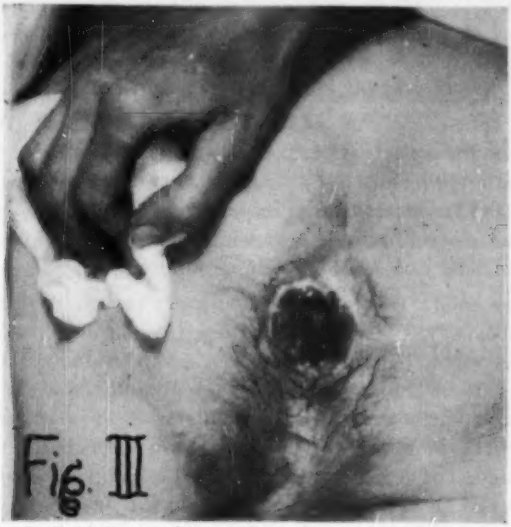

Fig. 3—Epithelioma arising on base of a posterior fissure in ano.

To be effective, the anal sphincter as well as the puborectalis muscle require actual stretching or attenuation. The degree of actual stretching under anesthesia is not easily determined. Partial or complete incontinence may result, particularly in older patients, and may be permanent. The subcutaneous external sphincter, because of its annular arrangement, requires much more attenuation than the other divisions of the external sphincter or the levator ani. This, no doubt, accounts for the effectiveness of the procedure in the relief of fissure and chronic anal spasm. The method, although not as safe or as effective as surgical excision, is indicated in the spastic, nervous type of individual who is intolerant to surgery and may be aggravated by it.

Divulsion should not be done under general or intravenous anesthesia. Spinal is most satisfactory, but the degree of relaxation which this type of anesthesia

affords must be sufficiently appreciated in this procedure. The method of gradual insertion of the index and middle fingers of each hand is usually effective. Stretching should be done very gradually and the muscles "ironed out" around the clock. The injection of Anucaine, as described above, prolongs the sphincter relief and permits a smoother postoperative course. In infancy or early childhood simple dilatation with the correction of dietary and bowel habits usually suffices for permanent cure. However, a fissure on the basis of anorectal malformation, e.g. marked stenosis, usually requires surgical correction.

Radical Excision:—This is the surest method of not only healing the fissure but also of restoring a normal function of the anal canal. It is emphasized again that in the chronic fissure, excision with continuous adequate drainage and the removal of associated pathology with complete division of the subcutaneous external sphincter muscle are necessary for permanent cure. The technic is simple but somewhat exacting.

Anesthesia:—Local, sacrocaudal, spinal or intravenous anesthesia may be used. We prefer a low spinal of 30 mg. of procaine through a small-gauged needle, e.g. #22. Regardless of the anesthesia and unless contraindicated, 15 cc. of Anucaine are injected into the perianal tissues. The use of the oil anesthesia prevents postoperative spasm and facilitates careful inspection of the upper angle of the wound. It is preferable to inject oil-soluble anesthetics before contaminating surgical procedures are begun. The jack-knife position is preferred.

Following anesthesia, the anal canal and lower rectum are carefully examined for associated pathology, e.g. large hemorrhoids, prolapsed mucosa, deep crypts, etc. A large hypertrophic papilla or polyp is a common finding and forms part of the pathology of chronic fissure. An occasional high-lying fissure is commonly overlooked. Adequate exposure is necessary and dilatation should be done accordingly. If exposure is not readily obtained by dilatation, the musculature should be incised without further ado. The fissure, together with the sentinel pile and sinus tract, if present, are removed en masse. Excision starts in the anal canal and is continued on either side freeing the entire fissure bed, and continuing posteriorly to include the sentinel pile and sinus tract. The lateral skin incisions are extended posteriorly for a distance of about 2 inches, excising triangular or racquet-shaped flaps of skin. The posterior margin of the skin wound should be on the same level as the excision of the sphincter in the anal canal. In obese individuals, the posterior wound should be somewhat wider and carried well posteriorly. The subcutaneous external sphincter with the intramuscular fibrosis (pectenosis) is now dealt with. It is important to determine the extent of the fibrosis and the degree of fixation of the posterior tissues. At times the fibrosis extends some distance around the anal canal in the intermuscular septum. In these cases it may be preferable to excise entirely a portion of the subcutaneous external sphincter muscle to secure adequate drainage. Complete division of the external sphincter muscle and the contracting fibrosis is the essential minimal requirement. The fibrosis may extend to the puborectalis level and at times it may be necessary to incise it and the profundus

portions of the external sphincter. This should be done gradually and under direct vision. A characteristic lack of resistance to the insertion of the index finger follows adequate division of the posterior tissues. No suturing of any pedicles is considered advisable. Any obstructions to free and adequate drainage are excised. This usually includes overlapping edges or large internal hemorrhoids. The mucosal flaps are excised, not tied off. The internal hemorrhoids are sometimes troublesome particularly if large external skin tags exist. In these cases excision of the skin tags may be made part of the larger fissure wound posteriorly or they may be excised separately with a small bridge of skin between the wounds. The stenotic features of a large, encircling posterior scar may negate the fissure surgery and require prolonged dilatation.

In order to assure further healing and avoid primary union or troublesome postoperative bridging, the fissure wound is firmly packed with 3 or 4 one-inch superimposed strips of iodoform gauze. This is most important. A small, soft rubber tube is placed in the rectum and vaseline gauze is placed between the skin edges to avoid adherence. Oxycel may be used for excessive oozing.

Anterior fissures usually require less surgery. To insure adequate drainage, however, the wound should be triangular and extended laterally, if necessary, in the female perineum.

In combined anterior and posterior fissures incision of the musculature is necessary only posteriorly, but both anterior and posterior skin drainage incisions are required. A contracted anus is sometimes associated with chronic fissure. It may be necessary in these cases to incise the posterior musculature to some depth. No definite rules can be advanced. Experience is essential. In these cases it may be advisable to undermine the rectal mucosa and suture it to the near-margins of the anal wounds. This procedure may lessen the chance for recurrence. The sphincterotomy must be deep enough to assure an adequate and nonobstructed anal outlet when healing is complete.

Postoperative Care

The Penrose drain or tube is removed on the first day. If the sphincter is completely incised the pain is distinctly less than after hemorrhoidectomy. The usual postoperative routine consists of adequate sedation, Sitz baths, and local heat. The bowels are moved on the morning of the third day following Sitz baths and local irrigation with potassium permanganate solution, 1:4000. The iodoform packing, if not passed in the first evacuation, is removed with the aid of peroxide and topocaine. The avoidance of bridging and deep pocketing is assured by the passage of a small dilator, e.g. finger or cotton applicator daily or every other day. Further healing depends on complete and adequate drainage. Sphincter relaxation is most important to avoid pooling of the secretions and wound pabulum. If there is any bridging or tendency to pocket at the rectal end of the incision, reconstruction of the wound should be done at once. It is essential that the anal end of the wound heal completely before the outer skin. Cauterization or coagulation may be

necessary to accomplish this or the skin may require further incision posteriorly and even laterally. The wound should assume a smooth, red, healthy granulated appearance about the fifth day, and the passage of a finger or dilator should not be unduly painful thereafter. If pain is present, ulceration rather than a clean granulating wound should be suspected. Painful ulceration results in excessive anal spasm, a precursor for recurrence. Occasionally, healing is retarded by irritating seepage from the vagina, infection by fungi, virus or bacteria. These wounds require careful regular inspection with the indicated measures to secure complete physiologic drainage with local bacteriocidal or stimulating agents as indicated.

Summary

A comprehensive outline dealing with etiology, pathogenesis, anatomic considerations, symptomatology, diagnosis, differential diagnosis, treatment—both surgical and nonsurgical—and postoperative care has been presented. In passing, we would lay particular stress on what we consider the most important point of surgical management of chronic fissure. We are thoroughly convinced that if incisional methods are indicated and used, the entire subcutaneous portion of the external sphincter muscle together with the fibrous tissues should be completely incised or excised. Not to do this leaves a portion of the subcutaneous external sphincter shelf or fibrous tissue which may be as disabling as, or even more than the original one, because the few circular fibres left may still form a narrow posterior constricting band. That the shelf of the subcutaneous external sphincter and the underlying fibrosis constitute the most important impediment to the healing of chronic fissure is shown by the fact that the majority of chronic fissures never heal or persistently recur until the shelf and fibrosis have been entirely incised or excised and the posterior tissues mobilized. This is singularly significant. Complete division of the subcutaneous external sphincter muscle or excision of the fibrosis together with a large posterior drainage incision constitutes the essential feature of chronic fissure surgery.

The objectives in surgical treatment of fissures are to straighten out the angle of the anorectal axis; in simple words, to have the fecal mass traverse the anal canal in a more vertical plane with no corners or "bars" to overcome, and to mobilize the posterior tissues thus decreasing the anal resistance. The properly reconstructed fissure patient should have a relaxed, dilatable, unobstructed anal canal through which the expulsive forces from above may easily pass a well-formed stool. There is scarcely a more grateful patient when these objectives have been secured, and often they can be secured only by proper surgery.

BIBLIOGRAPHY

Abel, A. L.: The Pecten: The Pecten Band: Pectenosis and Pectenotomy. The Lancet, (April), 1932.

Blaisdell, P. C.: Pathogenesis of Anal Fissure and Implications as to Treatment. Surg. Gynec. & Obs. **65**:672-677, (Nov.), 1937.

Gorsch, R. V.: Fissure in Ano—Its Pathogenesis and Treatment. Med. World, **56**:300-302, (May), 1938.

Gorsch, R. V.: Perineopelvic Anatomy. The Tilghman Co., New York, N. Y.

Levy, E.: Anorectal Musculature. Am. J. Surg., **34**:141, (Oct.), 1936.

Milligan, E. T. C., Morgan, C. N., Jones, L. E. and Officer, R.: Surgical Anatomy of the Anal Canal and Operative Treatment of Hemorrhoids. Lancet, **2**:1119-24, (Nov. 13), 1937.

OBSERVATIONS ON AN ISOLATED GASTRIC POUCH IN MAN*

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Much valuable information about gastric secretion in dogs has been obtained by the use of isolated gastric pouches as described originally by Pavlov[1]. In man, the secretory activity of the stomach has been studied by the customary methods of clinical gastric analysis, and in exceptional cases by observations on patients with gastric fistulae[2,3,4].

The use of an isolated gastric pouch presents certain advantages, inasmuch as it provides the entire secretion of a given part of the stomach, available continuously over long periods of time, and uncontaminated by food, saliva, or duodenal reflux. For these reasons it would seem that a long-term study of an isolated gastric pouch in the human subject would prove fruitful.

An opportunity to construct a gastric pouch in man is provided by the operation of two-stage gastrectomy (resection with exclusion) which is used in certain difficult cases of duodenal ulcer. The present paper reports the findings in a case in which this procedure was followed.

The patient, a man aged 21 years, was submitted to operation on 28 January 1948. Anterior and posterior duodenal ulcers were present, buried in an inflammatory mass and adherent to the pancreas. The duodenum was somewhat narrowed, and the stomach was considerably dilated. In view of the technical difficulty that would have been encountered in removing the ulcer-bearing portion of the duodenum it was decided to perform "resection with exclusion". With this purpose in view, the stomach was divided immediately proximal to the pylorus, and the distal end closed and enfolded. The greater curvature of the stomach was mobilised by division of the gastrocolic omentum to above the level of the lowest of the vasa brevia, and the stomach was cut across at this level. A loop of proximal jejunum, drawn up in front of the transverse colon, was anastomosed to the cut end of the stomach after the method of Polya.

Up to this point the orthodox procedure of gastrectomy had been followed. Now, however, the distal segment of the stomach was not discarded, but was retained. A cuff of its distal extremity was removed, (to eliminate the alkali-secreting pyloric antrum), and the remaining portion was closed at both ends to form an isolated pouch comprising rather less than the middle one-third of the whole stomach. Drainage of the pouch was provided by a self-retaining rubber catheter inserted near its greater curvature, and brought out through a stab incision in the abdominal wall. Care had been taken, when mobilising the lesser curvature, to preserve the left gastric artery and vein along with the main leash of vagus nerve fibres. In this way the blood and nerve supply to the pouch were preserved intact;

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it may be added that the presence of many nerve bundles of healthy appearance was eventually verified histologically. Observations on the secretion from this isolated pouch were made throughout the next 2½ months, and these form the substance of the present report. Finally, the second stage of the gastrectomy was completed on 14 April, when the ulcer-bearing area of the duodenum was excised, as also was the gastric pouch. It was found that the therapeutic object of the staged gastrectomy had been attained, for the inflammatory mass around the ulcers had almost completely resolved, allowing the proximal duodenum to be excised with great ease. At no time did the patient's condition cause the least anxiety, and his present health remains excellent.

During the period of observation the patient was afebrile. He was kept in bed for six weeks: after that he was encouraged to be active, and he gladly helped with the domestic work of the ward. After the first few days he was given a free choice of diet from the variety made available by the Dietetic Department of the hospital, and no attempt was made to restrict him to the bland food usually advised for ulcer patients. Fortunately he escaped the postprandial discomfort and sense of fullness which are often troublesome in early convalescence after gastrectomy, and the size of his meals did not require limitation. He developed a distaste for tobacco and while he was in the hospital smoked only part of a single cigarette. He had no access to alcohol. Finally, it should be pointed out that the patient was of a placid disposition. He occasionally confessed to boredom, but at no time did he show any sign of anger or resentment, and there was no opportunity for observing the effect of strong emotion on the pouch secretion.

It must be conceded that a pouch of the kind described has two features which distinguish it from a standard Pavlov pouch. Food passes directly from the proximal portion of the stomach into the jejunum without traversing the duodenum, and again the duodenum remains the site of chronic peptic ulceration. These conditions of experiment should be borne in mind, for it may be that they modify the behavior of the pouch.

Method of Collecting the Secretion

The secretion from the pouch was collected in hourly samples. Throughout each 60-minute period the secretion was allowed to drain freely into collecting bottles by way of the catheter and suitable tubing, and at the end of the period the pouch and tubing were emptied by a simple maneuvre. Gentle suction was applied to the pouch by "milking" the catheter, and this served to empty both the pouch and the catheter. The rubber tubing was then disconnected and emptied by blowing through it. The efficiency of this simple method of emptying the pouch later became suspect, but its reliability with reasonable limits was shown by direct experiment. The catheter was temporarily clamped. Known volumes of saline were injected through a needle puncture in the wall of the catheter, in such a way as to enter the pouch. After a brief pause the clamp was removed and the pouch

emptied as described. The agreement between the volumes of saline injected and withdrawn was as follows:—

Injected. (cc.)	Recovered. (cc.)
5	4.5
10	10.9
15	12.2
5	8.1
10	10.1
15	13.5

A Note on the Variability of Samples

The volume and acidity of the pouch secretion varied throughout the day, following, in the main, an easily recognized pattern. Superimposed on this pattern, however, there were occasional random fluctuations for which no cause could be found. Thus the rate of secretion by day was usually about 15 cc. per hour, but occasional samples were as small as 5 cc. or as large as 30 cc. At first these fluctuations were attributed to failure to secure complete emptying of the pouch, but this possibility was eliminated by the test described above. Moreover, it was soon found that anomalous samples tended to occur in sequence rather than singly, and that abnormalities in volume were usually accompanied by abnormalities in acidity. It was concluded, therefore, that the fluctuations were indicative of real variations in the activity of the pouch.

Results

1. *The long-term increase in the activity of the pouch:*—There was a slowly progressive increase in the activity of the pouch throughout the 2½ month period of observation. During the first fortnight the specimens obtained were thick, turbid, and sticky from their excessive content of mucus. From this time onwards the amount of mucus secreted was small: most of the specimens showed a faint opalescence, but many were crystal clear, especially when the rate of secretion was high. Acid was uniformly absent from the specimens collected during early convalescence, and titratable acid appeared for the first time on the 12th day. From this time, acid was invariably present, and in amounts which gradually but steadily increased. This gradual increase is well shown in Fig. 1 which represents the findings on 4 days chosen at spaced intervals. It will be seen that the mean acidity, which was zero for the first 12 days, had increased to the order of 30 clinical units (cc. N/10 acid per cent) by the end of 3 weeks, and increased further to the order of 100 clinical units by the end of 2½ months. The possibility that the acidity might have risen even further with more prolonged observation cannot be excluded, but during the last fortnight of observation there was no evidence of the rise being continued. As will be seen, the gradual increase in acidity throughout the period of observation was accompanied by a similar but less marked tendency towards an increase in the volume of juice secreted.

The very high acidity of the samples obtained towards the end of the period of observation should be borne in mind when interpreting the significance of the various tests carried out at that time. This point will be referred to specifically in the paragraphs dealing with the response to histamine and to insulin hypoglycemia.

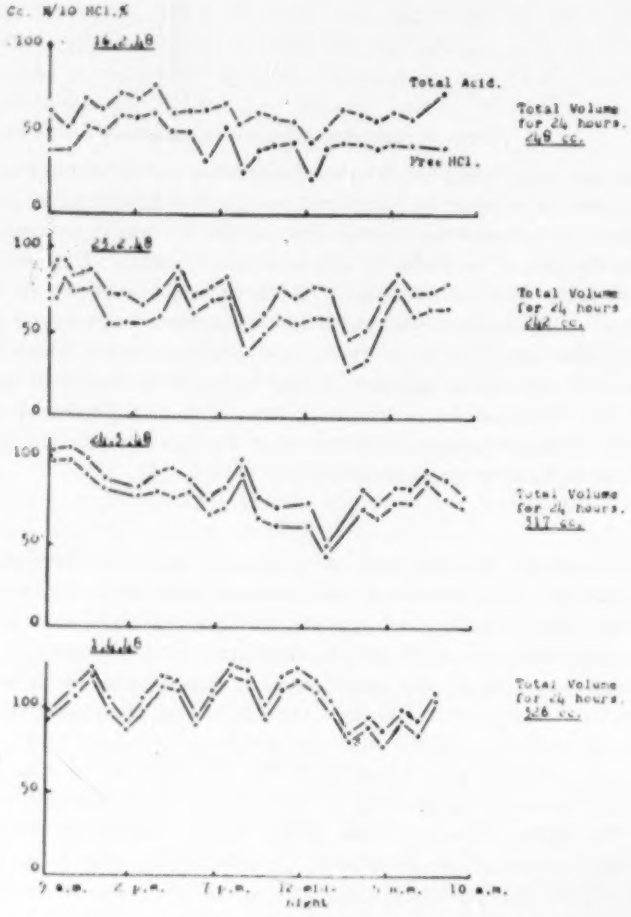

Fig. 1—To illustrate the increasing acidity and daily output throughout the 2½ months of observation.

2. *Daily variations in acidity and secretion rate:*—A daily cycle in the activity of the pouch was a prominent feature. Both the acidity and the rate of secretion tended to be higher by day than by night. This tendency is clearly shown in Fig. 2, which presents the records of 3 days on which the cycle was particularly obvious. In reading these graphs it should be borne in mind that under hospital

routine the patient settled down for the night between 8 and 9 p.m., and was wakened between 4 and 5 a.m. It will be clear, therefore, that the periods of high and low activity of the pouch correspond with periods of waking and sleeping. In this connection, the early morning increase in the acidity of the secretion deserves

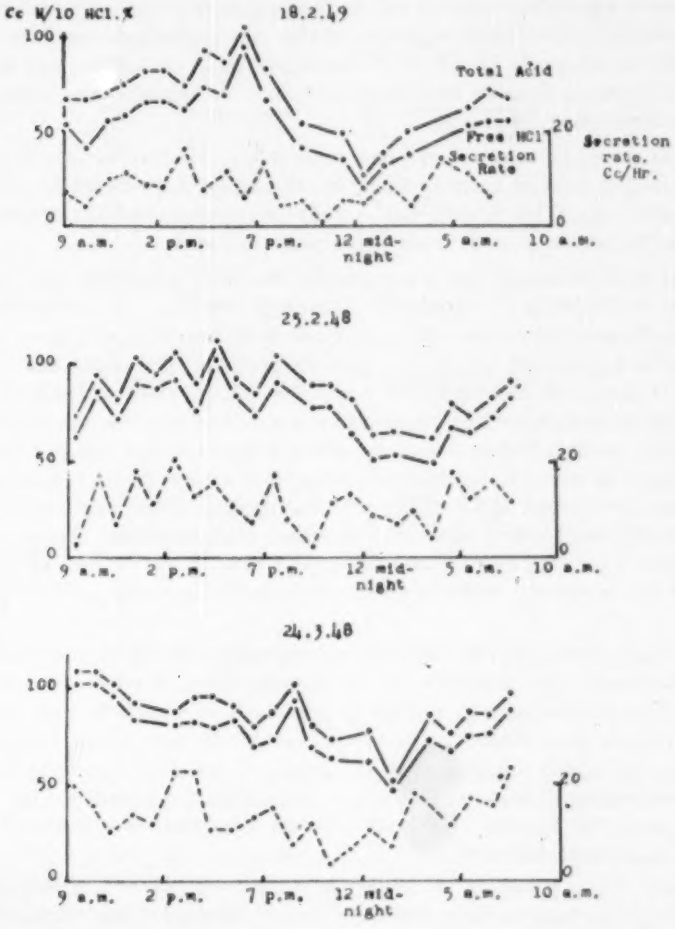

FIG. 2. To illustrate the reduction of secretory activity by night.

particular notice. Between the hours of 5 and 8 a.m. the patient was awake and, indeed, after the first six weeks was at this early hour assisting in the domestic work of the ward. His first meal was breakfast at 8 a.m., and he neither sought nor was offered an early morning snack. The early morning increase in the activity

of the pouch was, therefore, associated with the physical activity of the patient: it can hardly be attributed to hunger, as the patient never sought food, and it was certainly not a response to eating a meal.

It would be incorrect to suggest that the typical daily cycle in the activity of the pouch was to be found invariably. Exceptions were by no means rare, and some examples can be found elsewhere in this report. Reduced secretion at night was, however, observed on 17 of 25 occasions: on 8 occasions there was little difference between the day and night secretion: no instance was found of the night secretion being the greater.

3. *Absence of a secretory response after meals:*—It may be said at once that no postprandial increase could be found in the acidity of the pouch secretion or in the secretion rate. This finding was entirely unexpected, and the evidence upon which the statement is made is therefore given in detail.

In general, the absence of a postprandial increase in secretion can be verified from any of the diagrams reproduced throughout this paper. In interpreting them it is to be borne in mind that the main meals were breakfast at 8 a.m., dinner at noon, tea at 4 p.m., and supper at 6 p.m. In addition, the patient had a glass of milk at 11 a.m., and at bedtime (8 p.m.). On this program of frequent feeding a postprandial response might be somewhat masked during the course of the day, and for this reason attention should be directed chiefly to the first and last meals. The increase in secretory activity extending over several hours before breakfast has already been noted, and it will be seen that there is seldom any further increase (and certainly no acceleration of the increase) after breakfast. Again, despite a large supper at 6 p.m., and a glass of milk at 8 p.m., it will be seen that often by this time the secretory activity of the pouch is declining to the lower levels found at night.

In order to test out the possibilty of obtaining a secretory response to food under conditions most favorable for its demonstration, a group of observations was made on the response to a series of breakfasts of especially large size, given after a 12-hour fast. Half-a-dozen special breakfasts were given, comprising in duplicate, meals with a high content of protein, of fat, and of carbohydrate. The actual composition of these meals is given in detail in the legend of Fig. 3. It will be seen from the diagram that none of these breakfasts was followed by any material increase of secretion.

Finally, for a period of 36 hours the patient was given a continuous milk drip delivered by nasal catheter into the proximal remnant of the stomach. Despite this constant feeding, the pouch secretion followed the usual pattern of being greater by day than by night.

It was concluded that the absence of a secretory response after food, suggested by the protocols in general, was established by means of the special test breakfasts. Moreover, the results obtained while giving continous feeding with milk indicated that reduced secretory activity by night could not be attributed to fasting.

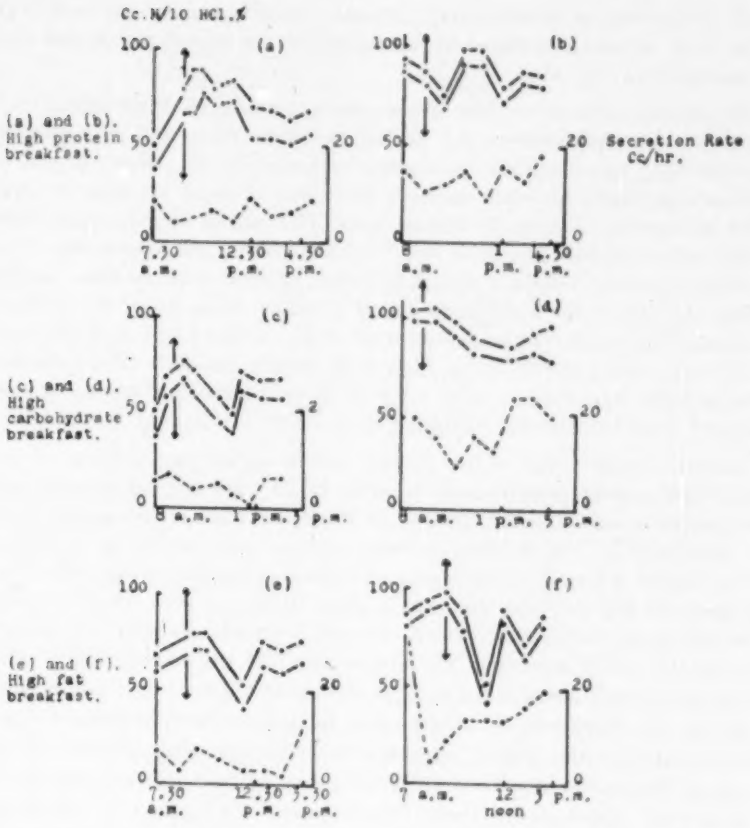

FIG. 3.

Fig. 3—To illustrate the effect of special breakfasts containing respectively a high content of protein, of fat, and of carbohydrate. Breakfasts given at 9 a.m. after a 12-hour fast.
The composition of the breakfasts was as follows.

(a) Egg, fish, milk, bread, butter, tea, sugar, skim milk, and dried skim milk; Calories 799; Carbohydrate 71, *Protein 68*, Fat 27 (stated in gm.).

(b) Steamed fish, toast, butter, skim milk, dried skim milk, sugar, tea; Cals. 352: C. 23, *P. 47*, F. 8.

(c) Oatmeal porridge, milk, bread, syrup, banana, tea, sugar; Cals. 908; *C. 203*, P. 15, F. 4.

(d) Lemon juice and glucose, corn flakes and milk, egg, bread, butter, jam, tea, sugar; Cals. 1064: *C. 183*, P. 20, F. 28.

(e) Scrambled egg, bread fried in fat, toast, butter, tea, milk, sugar: Cals. 960, C. 45, P. 15, *F. 80*.

(f) Scrambled egg and butter, bread fried in fat, toast, butter, tea, milk, sugar: Cals. 963: C. 49, P. 14, *F. 79*.

4. *The effects of administering histamine, insulin, and atropine:*—The effects on the pouch secretion produced by histamine, insulin hypoglycemia, and atropine are illustrated in Fig. 4.

Histamine:—Histamine was given subcutaneously on three occasions. The dose given was equivalent to 0.5 mg. of histamine base, and was sufficient to cause flushing, sweating, and headache. Nevertheless, the effect on the pouch secretion was slight. On each occasion there was a small increase in titratable acidity amounting to about 10 clinical units. The rate of secretion was increased on two occasions and decreased once. In interpreting the significance of these somewhat equivocal results it should be borne in mind that the tests were made towards the end of the 2½ month period of observation, when the spontaneous secretion of the pouch had a concentration of free hydrochloric acid of about 100 clinical units, which is perhaps as high as is usually observed after histamine. It would probably be correct to infer, not that histamine was ineffective, but that the conditions were unfavorable for obtaining a clearcut histamine response.

Insulin hypoglycemia:—The patient proved to be very tolerant of insulin. Soluble insulin given intravenously in doses of 20 units over 65 minutes, and 45 units over 48 minutes failed to reduce the blood sugar below 70 mg. per cent. The tests illustrated in Fig. 4 were, however, satisfactory, for by giving the large doses of insulin indicated in the legend, the blood sugar was brought down on one occasion to 42 mg. per cent, and on the other to 38 mg. per cent. This profound degree of hypoglycemia had, as will be seen from the diagram, no appreciable effect on the pouch secretion. The suggestion that the absence of a secretory response to hypoglycemia might indicate destruction of the vagal nerve supply to the pouch was considered to be untenable for the following reasons. Every care had been taken at the original operation to avoid damaging the leash of nerves running to the pouch: after removal of the pouch, nerve fibres were readily found by dissection: histologically these fibres showed no evidence of degeneration, (Fig. 5): and finally atropine (as will be shown below) retained an unequivocal depressant action. Probably the correct explanation of the failure to obtain a secretory response to hypoglycemia (like the failure to obtain a histamine response) was the high degree of spontaneous activity of the pouch.

Atropine:—The effect of atropine was tested on 5 occasions, the dose administered being 1/50 gr. of atropine sulphate by mouth. The effect is well illustrated in the pair of records reproduced in Fig. 4, where it will be seen that there was a fall both in titratable acid and in secretion rate, lasting approximately 2 hours. It may be added that reduced secretory activity was found on each of the 5 occasions when atropine was given. The ease with which hyposecretion could be demonstrated after atropine contrasts with the difficulty in demonstrating hypersecretion after histamine or hypoglycemia. It seems probable that the high degree of spontaneous secretory activity of the pouch provided conditions which were exceptionally favorable for demonstrating inhibition.

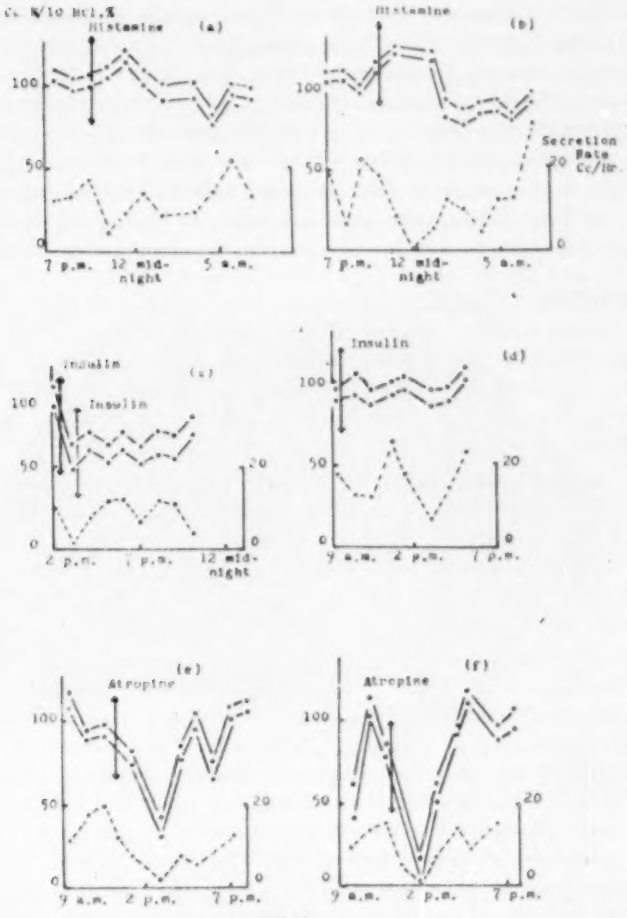

FIG. 4.

Fig. 4—To illustrate the effects of histamine, insulin hypoglycemia, and atropine. (a) and (b) effect of histamine, dose equivalent to 0.5 mg. histamine base given subcutaneously. (c) effect of intravenous soluble insulin 45 units followed by 30 units after an interval of 40 minutes, producing hypoglycemia with minimum blood sugar of 38 mgs. per cent. (d) effect of insulin 40 units with minimum blood sugar 42 mg. per cent. (e) and (f) effect of atropine, 1/50 gram atropine sulphate by mouth. In the text, reference is made to the dates of the tests which were:—

(a) 30 Mar. 48 (evening). (b) 8 Apr. 48. (c) 26 Feb. 48. (d) 7 Apr. 48. (e) 30 Mar. 48 (morning). (f) 27 Mar. 49.

5. *The effect of acidosis and alkalosis*:—Acidosis and alkalosis were induced for the purpose of observing their effect on the pouch secretion. Acidosis was induced by ammonium chloride (2 gm. doses given 6 times daily for 12 days), and alkalosis by sodium bicarbonate (4 gm. doses given 6 times daily for 5 days). Because interest centered on long-term rather than on hourly fluctuations, the pouch secretion was collected in pooled 24-hour samples. For the period of these tests the intake of food, water, and salt was kept constant.

The courses of medication described were sufficient to cause a considerable disturbance in fluid balance and acid-base balance. During the early stage of acidosis there was a pronounced diuresis resulting in a loss of body weight amounting to 1.5 Kg, and the pH of the urine fell to between 5.2 and 5.8. The pH of the blood, initially 7.65, fell gradually and somewhat irregularly to 7.4. Towards the end of the period vomiting became troublesome. During the alkalosis there was marked water retention and the body weight increased by 2.5 Kg (i.e. to 1 Kg in excess of the original weight). The pH of the urine increased to pH 8. The blood pH rose abruptly within one day from 7.4 to 7.65, and then more slowly to 7.7. Towards the end of the period headache became troublesome.

Despite these considerable changes in fluid and acid-base equilibrium, there was very little alteration in the secretion from the pouch. It will be seen from Fig. 6 that during the period of the acidosis the acidity and volume of the 24-hour specimens remained almost constant. During alkalosis there was an early reduction in both acidity and volume, but this was not maintained and the initial levels had been regained by the end of the period.

6. *A note on the peptic activity of the pouch secretion*:—Unfortunately no thorough investigation of the peptic activity of the pouch secretion could be undertaken because of the writer's difficulty in obtaining consistent results with an unfamiliar technic. Good agreement between tests in duplicate was obtained only on the last day on which the patient was available for study. The method of Anson (1938) was used, very slightly modified, and results are expressed in milligrams of tyrosine liberated by 0.02 cc. of gastric juice in 10 minutes at 25° C. from 2.5 per cent solution of human hemoglobin. The peptic activity of 5 random samples of the pouch secretion was 0.17, 0.22, 0.23, 0.25, and 0.41. For comparison the peptic activity of gastric juice obtained from two convalescent patients (following appendectomy and hemorrhoidectomy) was 0.08 and 0.11.

7. *A note on the absence of ulceration in the pouch*:—When the pouch was ultimately excised, the mucous membrane was carefully examined. There was no ulcer, and no evidence of inflammation on either naked-eye or on histological examination. It is of interest to note that the mucosa could tolerate without harm, continuous exposure for a period of 2½ months to a high and increasing concentration of acid.

Discussion

One of the chief aims of the present paper is to draw attention to the fact that the procedure of two-stage gastrectomy (occasionally resorted to in the

surgical management of difficult cases of duodenal ulcer) offers scope for the construction of isolated gastric pouches in man.

The observations upon an isolated gastric pouch in man reported here are believed to be the first of their kind. While the observations themselves are of a simple character, their significance is by no means easy to assess. In the first place, only further experience can show whether the results obtained are representative for this class of pouch. Again, the opportunity which allows of a pouch being constructed also imposes certain conditions of experiment which may influence the behavior of the pouch. Thus the first stage of a gastrectomy has necessarily been completed, and anastomosis of the proximal remnant of the stomach to the

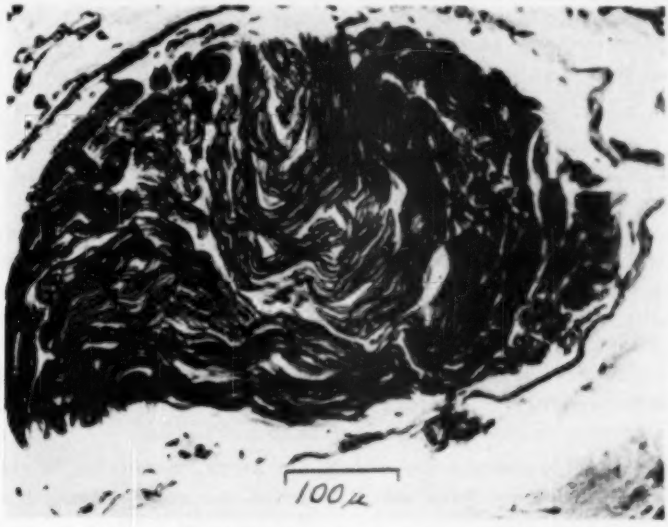

Fig. 5—To illustrate a nerve bundle in the pedicle of the pouch, showing normal architecture. Modified Bodian silver impregnation.

jejunum must allow food to pass out of the stomach with abnormal rapidity, and without coming into contact with the antral mucosa and duodenum. Again, the possibility exists that the presence of a chronic ulcer in the duodenum may itself modify gastric secretion. In view of these considerations it would be idle at the present stage to speculate on how closely the secretion from the pouch resembles secretion from the intact stomach. Accordingly, in the discussion which follows, no attempt is made to reach conclusions of general application.

A temporary disturbance of secretion from the pouch in the early postoperative phase was not unforeseen, but the gradual increase in secretory activity throughout the 2½ months of observation was unexpected and puzzling. No satisfactory explanation can be offered. The only explanation which appears to be even remotely plausible is that the blood supply to the pouch, initially inadequate for

supporting a highly active mucosa, slowly improved with the gradual enlargement of the vessels in the pedicle. However, experience of deliberate ligation of the gastric vessels, at one time advocated in the treatment of peptic ulcer, has shown that even when the blood supply has been compromised to an extent which appears alarming, the acidity of the gastric juices can return to normal within 4-6 weeks. In the present case, on the other hand, care had been taken to preserve the blood supply to the pouch, and as far as could be judged by the color of the pouch at the time of the operation the blood supply remained fully adequate.

Evidence has been presented that there was a daily cycle in the activity of the pouch, with a pronounced tendency to hyposecretion at night. The cause of this hyposecretion merits consideration, and in addition the findings in the present investigation require to be related to current views on secretion by the intact stomach.

The hyposecretion observed at night could possibly be attributed to overnight fasting. However, in the present patient no evidence was found of a relationship between meals and secretory activity. Moreover, with the object of eliminating the overnight fast, drip-feeding with milk was carried out for a period of 36 hours, and despite this continuous feeding the hyposecretion at night was still observed. It seems a more probable explanation that the reduction in functional activity of the stomach by night was part of the general reduction of bodily activity during sleep: the mechanism concerned might be diminished stimulation through the vagus, perhaps combined with a general diminution in the blood flow to viscera compensatory to the cutaneous vasodilatation well known to occur. The marked increase in secretory activity over the period of several hours when the patient was awake before breakfast, tends to confirm that the nightly hyposecretion should be associated with sleep rather than with fasting.

The relationship between the nightly hyposecretion observed in the present case and current views on basal gastric secretion in man, is somewhat uncertain. It is perhaps not generally realized how conflicting is the evidence on the secretion of acid by the fasting stomach in the human subject. Reviewing the literature in 1923, Carlson[3] concluded that in the opinion of most observers acid secretion was in abeyance during fasting, but expressed his own view that secretion continued at a reduced rate. Stressing the contradictory nature of the evidence, Babkin[6] in 1944 was forced to conclude that no decision could be reached whether acid secretion in man is continous or intermittent. A review of the literature would be out of place here, but the discrepancies among the views expressed can briefly be illustrated. Studying patients with gastric fistulae, Beaumont[2] and Wolf and Wolff[4] found acid secretion in abeyance during fasting, but Carlson[3] found that it continued at a reduced rate. Chalfen[7], who was a pioneer in the method of overnight intubation of the intact stomach, found secretion virtually in abeyance during sleep: as in the present study he noted that secretion gradually became more active on awakening. A year later, Polland and Bloomfield[8] reported that in most subjects the fasting secretion was copious, and indeed often more strongly acid

than the juice secreted in response to an Ewald test meal. Hellebrandt and others[9] studying healthy young women found secretion to be continuous with the peak acidity occurring at night; these authors also pointed out that the continuous fasting secretion was often more acid than the secretion after a test meal of gruel or alcohol. The investigation of gastric night secretion has received fresh impetus from the reintroduction of vagotomy in the treatment of peptic ulcer, and it is generally believed, not only that there is excessive night secretion in patients with duodenal ulcer, but that this hypersecretion is abolished by vagotomy: this opinion is ably championed by Dragstedt[10,11]. In contrast with this view, Sandweiss and others[12] found that in the absence of severe symptoms the night secretion in duodenal ulcer patients was no greater than in healthy subjects: they stressed the importance of continuous as opposed to hourly aspiration, so as to avoid fallacies of comparison arising from impaired emptying of the stomach in the presence of duodenal ulcer. The foregoing brief discussion may serve to indicate that studies of patients with gastric fistulae, and studies based on overnight aspiration of the gastric contents, have not clarified the question of the behavior of the

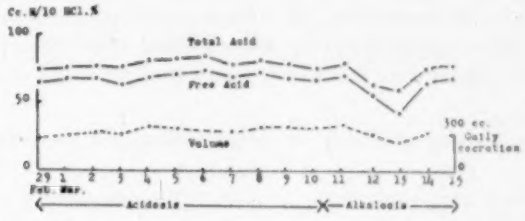

FIG. 6. To illustrate the change in secretion accompanying acidosis and alkalosis. Note that the acidity and volume refer to pooled 24 hour samples.

human stomach during fasting. It may well be that the solution of this problem must await the study of several examples of isolated gastric pouches, perhaps of the type described in this paper.

The entire absence of any increased secretion from the pouch after the ingestion of food was perhaps the most surprising of the observations made. It is at present generally accepted that a secretory response to food is as much a feature of gastric digestion in man as in the dog. Increased secretion after food has indeed been directly observed by those who have studied patients with gastric fistulae, and it is a commonplace clinical observation that the volume and acidity of the gastric contents increase markedly after the administration of a test meal. The possibility that this apparent increase in secretion might be illusory, and attributable to temporary closure of the pylorus (preventing alike the escape of gastric juice continuously secreted, and reflux of alkali from the duodenum) has been ably examined, notably by Ihre[13]. This worker, by means of triple intubation, recovered not only gastric juice for analysis but at the same time withdrew and discarded saliva and duodenal secretion, thereby appearing to eliminate all sources of error.

It seems almost incredible that a secretory response to food by the human stomach, substantiated by so much evidence, can seriously be contested. Nevertheless, workers already cited[8, 9] have demonstrated that there was no increase over the level of the fasting secretion following a test meal of gruel or of alcohol, which are routinely given in the confidence that they provoke gastric secretion. The failure in the present investigation to demonstrate a secretory response to food is therefore not a unique experience.

No success was obtained in demonstrating increased secretion after histamine or after insulin hypoglycemia. The interpretation offered for this finding is that the tests were carried out at a late stage in the period of observation, when the spontaneous activity of the pouch was already high, and conditions were consequently most unfavorable for demonstrating any pressor action. In contrast, the same conditions were exceptionally favorable for demonstrating inhibition. Indeed, it may perhaps be claimed that the present demonstration of the inhibitory action of atropine is at least as clear as any which has hitherto been offered.

Summary

An opportunity of constructing an isolated gastric pouch in man arose in the performance of two-stage gastrectomy for duodenal ulcer. Observations on the secretion from this pouch were made over a period of some 2½ months. The chief findings were:

1. Secretory activity gradually increased throughout the period of observation.

2. There was a daily cycle in the activity of the pouch, with a reduction both in acidity and in rate of secretion at night.

3. No secretory response after food could be demonstrated.

4. Histamine evoked a small increase in acidity: insulin hypoglycemia was without effect: atropine caused marked inhibition. However, spontaneous secretory activity was high at the time the tests were made.

5. Acidosis (induced by ammonium chloride) did not alter secretion: alkalosis (induced by sodium bicarbonate) led to transient hyposecretion.

These findings are briefly discussed.

Acknowledgments

For the opportunity to make this study, I am grateful to Professor C. F. W. Illingworth, who perceived that a routine staged gastrectomy offered scope for constructing an isolated pouch in man, and who carried out the operations described. During the period of acidosis and alkalosis the patient was in the care of Dr. James Reid of the Department of Medicine, University of Glasgow: throughout the investigation, Dr. Reid kindly gave laboratory facilities.

References

1. (Pavlov I.), Pawlow, J. P.: The work of the digestive glands. English translation by W. H. Thompson. Griffin & Co., London, 1902.

2. Beaumont, W.: Experiments and observations on the gastric juice, and the physiology of digestion. (1838 edition: Machlachlan and Stewart: Edinburgh).
3. Carlson, A. J.: Physiol. Rev. **3**:1, 1923.
4. Wolf, S. and Wolff, H. G.: Human gastric function: an experimental study of man and his stomach. Oxford University Press, New York, 1943.
5. Anson, M. L.: J. Gen. Physiol. **22**:79, 1938.
6. Babkin, B. P.: Secretory mechanism of the digestive glands. Hoeber, New York, 1944.
7. Chalfen, Sch. S.: Arch. f. Verdauungs-Krankheiten. **47**:106, 1930.
8. Polland, W. S. and Bloomfield, A. L.: Bull. Johns Hopkins Hosp. **49**:302, 1931.
9. Hellebrandt, F. A., Tepper, R. H., Grant, H. and Catherwood, R.: Am. J. Digest. Dis. and Nutr. **3**:477, 1937.
10. Dragstedt, L. R. and Owens, F. M.: Proc. Soc. Exp. Biol. **53**:152, 1943.
11. Dragstedt, L. R. and Schafer, P. W.: Surg. **17**:742, 1945.
12. Sandweiss, D. J., Friedman, M. H. F., Sugarman, M. H. and Podolsky, H. M.: Gastroenterology. **7**:38, 1946.
13. Ihre, B.: Acta. Med. Scandinav. Suppl. 95-96, 1938.

CHAPTER ACTIVITIES

Milwaukee Chapter

On 11 January 1950 the Milwaukee Chapter of the National Gastroenterological Association will celebrate its 15th year of organization. Following the annual dinner the Chapter will adjourn for a social evening in recognition of this event. Through the years the Chapter members have maintained a close and extremely friendly relationship amongst the rather small membership of ten.

The Officers for the year 1950 are President, Dr. C. J. Corcoran; Vice-President, Dr. I. I. Cash; Secretary-Treasurer, Dr. Michael W. Shutkin.

New York Chapter

Dr. Franz J. Lust, chairman of the Program Committee of the New York Chapter of the National Gastroenterological Association announces that the first clinical session of the Chapter will be held on Monday evening, 10 April 1950 at the New York Academy of Medicine.

The purpose of this clinical meeting is to acquaint members of the Chapter with the professional work of the other members and to give those who so desire, a chance to present original and interesting clinical cases.

Presentation of these cases is limited to members of the New York Chapter and each will be for a period of ten minutes. Those who are interested are urged to communicate with Dr. Franz J. Lust, chairman of the Chapter Program Committee, 15 East 89th Street, New York 28, N. Y.

NEWS NOTES

Executive Board Meeting

A meeting of the Executive Board of the National Gastroenterological Association was held at the Hotel Statler in New York City on Sunday, 20 November 1949.

Following the disposal of routine administrative correspondence and reports, Dr. Roy Upham, Secretary-General reported that the New York Chapter had held a meeting at the New York Academy of Medicine on 14 November 1949 and that the next scheduled meeting was to be held on 9 January 1950.

Upon recommendation of the Boston, New York and Uruguay Chapters the applications for the following members were accepted by the National Executive Board: Dr. Joseph P. Kvaraceus, Brockton, Mass., Member; Dr. William Peter Mavraides, Jamaica Plain, Mass., Member; Dr. H. Allan Novack, Boston, Mass., Member; Dr. Alfred L. Solow, Wollaston, Mass., Member; Dr. Seymour Albert Fink, New York, N. Y., Member; Dr. Charles David Karutz, Ridgewood, N. Y., Member; Dr. Rudolph Nissen, New York, N. Y., Associate Fellow; Dr. Joseph Roger Van Dyne, Forest Hills, N. Y., Member; Dr. Tomas Clivio Durante, Montevideo, Uruguay, Member.

The following were elected to membership at large in the National Gastroenterological Association: Dr. Joseph P. Cangelosi, Chicago, Ill., Member; Dr. William Edgar Jones, Texarkana, Texas, Fellow; Dr. C. W. McNamara, Toledo, Ohio, Fellow; Dr. Michael A. Michaels, Manchester, N. H., Member; Dr. J. B. Michaud, Drummondville, Quebec, Member; Dr. Samuel Joseph Nigro, Chicago, Ill., Member; Dr. Francis B. Tabaka, Chicago, Ill., Member and Dr. Cecil E. Tate, Jackson, Michigan, Member.

The Board set definite dates for future meetings in order to permit out-of-town members to attend more frequently.

The selection of a Convention site for 1951 was again discussed and the cities of Detroit, Montreal, Baltimore and Boston were considered. This matter was referred to the Convention Committee with instructions to report back to the Executive Board at its next meeting.

The matter of appointing a Convention Manager for future Conventions was presented and it was agreed that such an appointment is desirable in the light of lessons learned at the last Convention. The matter was taken under consideration and referred to the President for appropriate action.

The Postgraduate Course for 1950 was discussed and it was agreed to hold it at the Hotel rather than at a Hospital immediately following the Convention session.

Dr. Horace W. Soper, President, submitted for the approval of the Board the names of members to be appointed to the various standing committees.

The Board voted that in the future all certificates would be awarded only at the time and place of the Convocation Ceremony which will be held in conjunction with the Annual Convention.

Following lunch the Board sat as a Committee of a Whole to revise the Constitution and By-Laws.

Standing Committees

Dr. Horace W. Soper, President of the National Gastroenterological Association, with the approval of the National Executive Board has appointed the following Standing Committees for the year 1949-1950.

Program Committee:—Dr. Anthony Bassler, chairman; Dr. Horace W. Soper; Dr. William R. Morrison; Dr. Samuel Weiss and Dr. Roy Upham.

Membership Committee:—Dr. William C. Jacobson, chairman; Dr. F. H. Voss; Dr. Benjamin M. Bernstein.

Nominating Committee:—Dr. Roy Upham, chairman; Dr. Felix Cunha; Dr. John E. Cox; Dr. Donald C. Collins.

Editorial and Publication Committee:—Dr. Samuel Weiss, chairman; Dr. Anthony Bassler; Dr. Harry M. Eberhard; Dr. William W. Lermann.

Endowment Fund Committee:—Dr. Horace W. Soper, chairman; Dr. Sigurd W. Johnsen; Dr. Elihu Katz; Dr. Henry A. Rafsky.

Research Committee:—Dr. Henry A. Rafsky, chairman; Dr. J. A. Campbell; Dr. A. X. Rossien; Dr. David A. Sandweiss; Dr. H. Necheles.

Convention Committee:—Dr. Horace W. Soper, chairman; Dr. Elihu Katz; Dr. Sigurd W. Johnsen; Dr. Anthony Bassler; Dr. Roy Upham.

Oral Examinations in the Subspecialty of Gastroenterology

The American Board of Internal Medicine announces oral examinations in the subspecialty of Gastroenterology to be held as follows:

10, 11 February 1950 at Chicago, Ill.
14, 15 April 1950 at Boston, Mass.
23, 24 June at San Francisco, Calif.

These examinations are for candidates who have been certified in Internal Medicine and who have made application and passed the requirements for examination in Gastroenterology.

Further information can be obtained by writing to Dr. William A. Werrell, Assistant Secretary-Treasurer, 1 West Main Street, Madison 3, Wisconsin.

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Mississippi Valley Medical Society 1950 Essay Contest

The Tenth Annual Essay Contest of the Mississippi Valley Medical Society will be held in 1950. The Society will offer a cash prize of $100.00, a gold medal, and a certificate of award for the best unpublished essay on any subject of general medical interest (including medical economics and education) and practical value to the general practitioner of medicine. Certificates of merit may also be granted to the physicians whose essays are rated second and third best. Contestants must be members of the American Medical Association who are residents and citizens of the United States. The winner will be invited to present his contribution before the Fifteenth Annual Meeting of the Mississippi Valley Medical Society to be held in Springfield, Ill., Sept. 27, 28, 29, 1950, the Society reserving the exclusive right to first publish the essay in its official publication—the Mississippi Valley Medical Journal (incorporating the Radiologic Review). All contributions shall be typewritten in English in manuscript form, submitted in five copies, not to exceed 5,000 words, and must be received not later than May 1, 1950. The winning essays in the 1949 contest appear in the January 1950 issue of the Mississippi Valley Medical Journal (Quincy, Illinois).

Further details may be secured from Harold Swanberg, M.D., Secretary, Mississippi Valley Medical Society, 209-224 W. C. U. Building, Quincy, Illinois.

ABSTRACTS

GASTROINTESTINAL TRACT

MASS ROENTGENOLOGICAL SURVEY OF THE GASTROINTESTINAL TRACT TO DETECT CANCER OF THE STOMACH. Sherwood Moore. Am. J. Roentgenol. 61:470, (April), 1949.

Moore concludes that with the present state of the art of gastrointestinal examination it must still remain an art and is therefore not suitable for mechanization such as would be the case with mass survey technics. Although there might be some possibility of detecting cancer of the stomach with this method, it probably would detect only the late cases. The accepted method of examination by the radiologists of this country is highly efficient, and gastric cancer of the one type which seems to be suitable for detection by mass survey methods comprises but a small part of the incidence of gastrointestinal cancer. From the data which have been accumulated, it is obvious that overemphasis has been placed on the incidence of cancer of the stomach. FRANZ J. LUST

KAPOSI'S SARCOMA. William H. Boone and Emil A. Kratzman. Am. J. Roentgenol. 61:511, (April), 1949.

Kaposi's sarcoma, or multiple idiopathic hemorrhagic sarcoma, is an unusual disease among adults in America. Boone and Kratzman report two cases with involvement of the small intestines. The clinical signs for involvement of the gastrointestinal tract were those of intestinal bleeding. The roentgenological findings were those of multiple papillary or polypoid lesions of the small intestines. The etiology of the disease is unknown. The disease is usually first manifested by skin lesions but cases are reported in which visceral lesions have preceded cutaneous manifestations. Practically all authorities agree that roentgen therapy probably gives the best results in treatment of the disease, but this is palliative. It is the early vascular lesion that usually responds to small doses of low voltage roentgen therapy, while the later type of lesion is much more resistant to treatment. Most of the lesions can be made to disappear with moderately heavy radiation dosage.
FRANZ J. LUST

STOMACH

THE NOCTURNAL GASTRIC SECRETION IN PATIENTS WITH BENIGN GASTRIC ULCER. Erwin Levin, Joseph B. Kirsner, Walter Lincoln Palmer. Ann. Int. Med. 30:1020-1032, (May), 1949.

Levin, Kirsner, Palmer and their associates have contributed much interesting information concerning continuous and nocturnal gastric secretion in normal persons, and patients with duodenal ulcer and those with gastric ulcer. In their previous paper, these authors reported the results of studies on nocturnal secretion of normal individuals and of patients with duodenal ulcer, gastric ulcer and gastric carcinoma. In the present publication the authors describe in clear detail the periodicity and variability of the nocturnal gastric secretion in these patients and compare them with normal subjects and patients with duodenal ulcer.

Here report is made of 57 observations obtained in 25 patients with benign gastric ulcer. In these patients there is apparently continuous gastric secretion although secretion of hydrochloric acid is not continuous. The volume of secretion and acid output are higher during the first half of the night. The rate of gastric secretion varies from hour to hour.

The acid output in the fasting nocturnal gastric secretion is lower in gastric ulcer than in duodenal ulcer patients. The concentration of free hydrochloric acid and acid-output are lower in gastric ulcer patients than in normal individuals. HYMAN I. GOLDSTEIN

PHYSIOLOGIC CHANGES FOLLOWING VAGOTOMY FOR PEPTIC ULCER. R. A. Griswold. South. Surgeon. 15:1-8, (Jan.), 1949.

Since Dragstedt revived the operation of vagotomy in the treatment of intractable ulcer (1943-1944) many hundreds of patients have been operated upon by this method. Vagotomy, or better, vagus resection (vagectomy) for peptic ulcer has been tried at various clinics here, and in Italy, France, and Germany during the past several decades.

Peptic ulcer is due to disordered gastric physiology rather than to infection or trauma. Disordered physiology of the gastric secretory mechanism produces chronic peptic ulcer in human beings. In many cases abnormal psychosomatic factors may cause the disordered physiology. The increased ability of the gastric juice to digest the mucosa of the gastrointestinal tract causes the chronic recurring ulcer.

Acidity and peptic activity of the gastric juice are the important factors i.e., the proteolytic action of pepsin when activated by the hydrochloric acid is what we are really thinking of in this problem. Peptic ulcer is primarily a medical disease. It is not surgical until the patient has had adequate medical therapy, except for acute emergencies, when surgical intervention is imperative.

It is probable that vagal secretion on the fasting stomach is more important in the production of ulcer than the humoral secretion. Humoral secretion is likely to be neutralized and diluted by food, and buffer substances. Most of the treatment of peptic ulcer has been directed toward reducing the peptic activity of the secretion by neutralizing the acid factor and preventing activation of the pepsin.

Gastroenterostomy cures about 75 to 85 per cent of ulcers without recurrence or gastrojejunal ulcers. Subtotal gastric resection cures about 90 to 95 per cent of ulcers (in patients who survive the operation!). Vagotomy or vagus resection will cure about 90 to 95 per cent—about the same cure-rate as for gastric resection. Vagotomy and gastric resection have certain undesirable side-effects: dumping-syndrome, difficulty in emptying the stomach, retention of food, and diarrhea.

The acid secretion is decreased by vagotomy. The secretory rate, due to vagal stimulation decreases following vagotomy. Emptying rate likewise decreases since this is a function of the motor activity of the stomach. There is also a marked decrease in concentration of acid, and pepsin in the gastric secretion.

Because of the decreased muscular activity of the stomach, vagotomy can convert incomplete retention into relatively complete retention. The author advocates drainage operations on all patients who have retained barium in the stomach at the end of 2 and a half hours because this suggests partial obstruction, and this (prevagotomy) partial obstruction may be made complete by reducing the propulsive power of the stomach after vagotomy. HYMAN I. GOLDSTEIN

ACCURACY OF ROENTGEN DIAGNOSIS OF BENIGN GASTRIC ULCER. C. A. Stevenson and C. W. Yates. Radiology. 52:633, (May), 1949.

The experienced radiologist is able to be highly accurate in the diagnosis of benign gastric ulcer. In a series of 91 adequately followed gastric ulcer patients, the roentgenological report of a benign lesion was accurate in 93.4 per cent. In spite of various criteria for the differential diagnosis between benign gastric ulcer and gastric carcinoma, we are unable, on reviewing the roentgenograms and the fluoroscopic findings, to find any difference in the six malignant cases erroneously diagnosed as benign ulcers in this series. We believe, therefore, that it is impossible, at any one roentgenological examination, to definitely differentiate a gastric ulcer from a gastric carcinoma. No particular fault can be found from a roentgenologic standpoint with either the medical or surgical procedures needed to enhance the accuracy of the roentgenologic diagnosis. However, since gastric carcinoma implies a very poor prognosis, it may be wise to consider seriously immediate surgery for all cases of roentgenologically diagnosed benign gastric ulcer, in the hope of early removal of the carcinoma in the approximately 10 per cent of cases in which the diagnosis is wrong. FRANZ J. LUST

GASTRIC RESECTION. THE SHOEMAKER—BILLROTH I. OPERATION. J. F. Higginson and O. T. Clagett. Surgery. 24:613-620, (Oct.), 1948.

The authors state the Shoemaker modification of the Billroth I operation permits greater, more extensive, resection of the lesser curvature of the stomach than other similar operations (Hoffmeister-Polya operation, etc.).

They report the immediate results of the Shoemaker-Billroth I technic in 95 cases. They prefer gastroduodenostomy to gastrojejunostomy because the former results in greater comfort and better, more efficient, physiologic activity, and maintenance of body weight. They believe the narrow stoma of a Shoemaker-Billroth I or a Hoffmeister-Polya anastomosis, from a physiologic standpoint, seems better than the wide stoma of a full Polya anastomosis.

The Shoemaker-Billroth I anastomosis seems better than the Hoffmeister-Polya—because of the small stoma, and the reconstruction of normal continuity by gastroduodenostomy, return the duodenum and the stomach as nearly as possible to normal physiologic activity. It is argued that postoperative gastric retention is more apt to occur with the small stoma, than with the larger stoma of the posterior Polya operation. HYMAN I. GOLDSTEIN

INTESTINES

POLYPOID DISEASE OF THE COLON. Louis A. Buie. Postgrad. Med. 177-183, (May), 1949.

In this article the author states that twelve to fourteen per cent of people over 40 years of age have polyps in their colons. All polyps of the colon must receive attention. Thirty per cent

of these polypi in the colon cannot be detected with the sigmoidoscope and may be missed. A barium enema may miss them. The author makes the statement that all polyps of the colon are cancerous, or will become cancerous if they are not destroyed and if the patient lives long enough. He also states that 25 per cent of patients with cancer of the colon have polyps in the adjacent tissue to the cancer. The most important question concerning polypoid disease of the colon is not *whether* something should be done, but *what* should be done. Half the polyps of the colon are small sessile outgrowths, discovered on routine sigmoidoscopic examination and bear no relationship to the chief complaint of the patient.

The author then goes on to discuss the treatment of these polyps. Pedunculated polyps should be fulgurized. Diffuse polyposis should be fulgurized only when surgery is contraindicated. Multiple polyposis should be treated by the removal of the colon which is not accessible to the proctoscope, then fulguration of the lower colon. Then an ileosigmoidostomy is done. The author concludes that the physician is never justified in releasing the patient from observation once a polyp has been discovered. The host must be periodically re-examined, whether or not symptoms are present.

LIONEL MARKS

PATHOLOGY AND LABORATORY RESEARCH

INCREASED SUGAR TOLERANCE AS A FACTOR IN THE PRODUCTION OF A SYMPTOM COMPLEX SIMULATING PEPTIC ULCER, NEUROCIRCULATORY ASTHENIA AND PSYCHONEUROSIS. Robert A. Peskin. Am. J. Digest. Dis. 15:92, (March), 1948.

Four cases are presented in which vague symptoms of a bizarre character were experienced for four years. In some, there is a family history of similar complaints. These symptoms were: hunger pains relieved by food, nervousness, apprehension, weakness in the legs, tremors, excessive perspiration, and mental dullness. The symptoms were aggravated or precipitated by physical effort and were prevented or relieved by eating and rest. The similarity of the group of symptoms, to symptoms associated with peptic ulcer, neurocirculatory asthenia, or psychoneurosis is discussed. The disclosure of the true cause for these symptoms by a study of the sugar tolerance, suggested itself from the similarity of these symptoms to those of hypoglycemia. Study of the blood sugar level at which symptoms of mild hypoglycemia occurred, revealed that these patients displayed symptoms at a relatively high sugar level. Confirmation of the observation that these patients' symptoms are due to relative hypoglycemia, was revealed by reproduction of the same symptoms with insulin and exercise. At a relatively high blood sugar level (88 mg. per cent) one patient began to have symptoms of tremor, air hunger and peculiar discomfort in the pit of his abdomen. More severe symptoms were evident at 74 mg. per cent. A disappearance of symptoms took place with the administration of orange juice. The value of high fat and protein diet in the prevention and relief of this metabolic disturbance is discussed. The practical value of the search for this entity in such obscure cases as neurocirculatory asthenia, psychoneurosis, and peptic ulcer syndrome without positive x-ray findings, is discussed. These patients disclosed mild liver and thyroid dysfunction. The concept that mild symptoms of hypoglycemia may appear at a relatively high sugar level is stressed.

FRANZ J. LUST

CANCER OF THE COLON AND RECTUM. O. H. Wangensteen. Wisconsin M. J. 48:591-597, (July), 1949.

In the male, the colon and rectum is the most frequent site for cancer. In the female, these sites are superseded by cancer of the breast and uterus. When the lesion is local, cancer is curable, and in cancer of the colon and rectum curability is greatest if the lesion is removed when there is no lymphnode involvement.

Rectal examinations must be a routine part of every physical examination with experience teaching that it is best "to think the worst in contemplating the diagnostic possibilities". Rectal bleeding must not be assumed as having only a hemorrhoidal origin. Sigmoidoscopic examination should be carried out by those qualified, after thorough cleansing of the colon and rectum. Besides lesions of the rectum, this examination may detect lesions in the sigmoid loop. Colic lesions are best detected by barium colon enema which should always be accompanied by air contrast studies.

The rectal and colonic mucosa do have a polyp-bearing area. Familial polyposis is rare; multiple cancers eventually develop after puberty. The author believes that there is little justification to await cancer before complete extirpation of the entire colon and rectal mucosa is carried out in cases of multiple polyposis. Polyps in the colon or rectum must be regarded as precursors of cancer with the ordinary colic polyp becoming malignant in approximately two years.

Cancers between the hepatic flexure and the lower limits of the sigmoid colon require colectomy with anastomosis of the ileum to the iliac colon. If the cecum and/or the ascending colon is involved, they are removed along with adjacent ileal coils and the adjacent lymphnode.

Lymphnode involvement does unfavorably influence the prognosis. In cases of Dukes' Group "C" the abdomen should be reentered for removal of gross lymphnode involvement three to four months after initial operation. This increases the cure rate of the aforementioned group. Isolated hepatic metastases should be excised at the first or second operation. Ordinarily, in hepatic excision, the problem of hemostasis is inconsequential.

The author discusses obstruction secondary to cancer and describes several technics of extirpating the underlined cause. He further strongly advocates cancer detection clinics and believes that every patient having cancer should be informed of his disease. A. X. Rossiter

PANCREAS

PANCREATIC CALCIFICATION. STUDY OF CLINICAL AND ROENTGENOLOGIC DATA ON 39 CASES. E. E. Gambill and D. G. Pugh. Arch. Int. Med. 81:301-315, (March), 1948.

The authors refer to calcareous deposits in the pancreas either within the ducts or in the parenchymatous tissue outside the ducts or in both. They refrain from using the term "calculi".

The authors studied the symptomatology, and the roentgenologic features in these cases and the incidence of diabetes mellitus and steatorrhea. There are no symptoms or signs by which pancreatic calcification can be diagnosed. Such diagnosis is a matter of roentgenologic study in the absence of surgical or postmortem examination. Among their cases two pseudocysts were found. The incidence of diabetes and steatorrhea in these cases was much greater when pancreatitis (chronic recurring) was present, than among patients who did not give a history suggestive of pancreatitis.

In 11 cases in which calcification involved the entire pancreas there were 9 instances of diabetes or steatorrhea. The treatment of pancreatic calcification is primarily that employed for the treatment of pancreatitis, which is the most common precursor of calcification. Medical treatment is ineffective. Surgical intervention was carried out in 18 of 39 cases of this series because of painful seizures, obstruction of the duodenum or common bile duct (due to enlarged pancreas), large calcareous masses interfering with pancreatic duct, or to drain or remove pseudocysts or abscesses of the pancreas. Calcareous deposits were usually found associated with relapsing pancreatitis. Among the associated complications were diabetes, steatorrhea, gastrointestinal hemorrhage, morphinism, pseudocysts, abscess and peripheral neuritis. Hyman I. Goldstein

BOOK REVIEWS

VASCULAR DISEASE IN CLINICAL PRACTICE. Irving Sherwood Wright, M.D., Associate Professor of Clinical Medicine, Cornell University Medical College; Chief of Section on Vascular Diseases of the Department of Medicine, New York Hospital. 514 pages. The Year Book Publishers, Inc., Chicago, 1949. Price $7.50.

The author has been actively interested in the field of peripheral vascular diseases, and in anticoagulant therapy for sometime. In recent years he has been almost entirely occupied in this special work both in private practice, in the hospital clinics, and in the work of the American Heart Association. He is one of that comparatively small, but important group who have contributed so much of value to this important special branch of medicine.

In recent years several large texts on the subject have appeared and have been justly well received. This smaller work by Dr. Wright contains, between its covers very informative and most instructive materials. This work is easy to read and to understand. Medical students, residents, internes, general practitioners, and junior staff men will benefit much by carefully studying the contents of this volume.

The study of the patient is clearly explained in 73 pages. Arteriosclerosis obliterans is presented in 114 pages. Consideration is given to Raynaud's Syndrome (1862), scleroderma, calcinosis, essential polyarteritis, scalenus anticus syndrome, hyperabduction syndrome, frostbite—seven and one-half pages are devoted to aneurysms—trench foot, acrocyanosis, thrombophlebitis and pulmonary embolism (49 pages), acute venous thrombosis (axillary or subclavian), telangiectasia, glomus tumors, are briefly but adequately presented. There is a chapter on medicolegal medicine, and an appendix on "Method for Determining Plasma Prothrombin". This work is recommended as the best practical presentation of the subject in a small compact volume.

CANCER OF THE ESOPHAGUS AND GASTRIC CARDIA. Edited by George T. Pack, B.S., M.D., New York, Clinical Professor of Surgery, New York Medical College, Attending Surgeon the Memorial Hospital for Cancer and Allied Diseases. Illustrated, 192 pages. C. V. Mosby Co., St. Louis, Mo., 1949. Price $5.00.

This excellent up-to-date little volume contains a symposium of the contributions by several experts which originally appeared in "Surgery" in June 1948 edited by Drs. Owen Wangensteen

and Alton J. Ochsner. Dr. George T. Pack contributes the introduction giving the historical aspect and the story, of the progress made in the surgical management of cancer of the esophagus and gastric cardia, from 1904 to 1948. Dr. Pack with Dr. McNeer also contributes the chapter on "Surgical Treatment of Cancer of the Gastric Cardia" (pp 145-188, with 86 references).

Robert S. Sherman writes on "The Roentgen Diagnosis of Cancer of the Cardiac Region of the Stomach" (pp. 16-25).

"Preoperative, operative, and postoperative care in esophageal resections" is ably and informatively treated by H. C. Maier. Watson and Pool contribute a chapter on "Cancer of the Cervical Esophagus", which covers the subject adequately and satisfactorily. They refer to the first successful human extirpation of the cervical esophagus for cancer, by Czerny in 1877. The patient dies of recurrent cancer fifteen months after the operation. Mikulicz' (1884) patient lived sixteen months after his operation, resection of the cervical esophagus and a plastic flap repair of the fistula, which permitted the patient to eat solid food ten days after operation. Garlock, of Mt. Sinai Hospital, N. Y. discusses the "Progress in the Surgical Treatment of Carcinoma of the Esophagus and Upper Stomach".

Other well known contributors are DeBakey and Ochsner of New Orleans, Macmanus of Buffalo, Richard H. Sweet of Boston and Reynolds and Young, Jr. of Chicago.

This small volume contains between its covers, valuable and authoritative information on the subject, and is deserving of high recommendation. Gastroenterologists and surgeons should find its contents of great interest.

MEDICINE THROUGHOUT ANTIQUITY. Benjamin Lee Gordon, M.D., Attending Ophthalmologist to Shore Memorial Hospital, Somers Point, N. J. and to Atlantic County Hospital for Tuberculous Diseases. Foreword by Max Neuburger, M.D. 818 pages, 157 illustrations. F. A. Davis Company, Philadelphia, Pa., 1949. Price $6.00.

This is a fascinatingly interesting account of medicine through the ages. The author, who is an experienced ophthalmologist, Hebrew scholar, and medical historian, is to be commended for a difficult labor of love, resulting in a very readable volume.

This book does present a well-woven story of medicine as it was developed and practiced by various peoples of the earth—"Prehistoric and protohistoric periods"—and the "Greco-Roman Period", as well as "Ancient Hebrew Medicine" are adequately and instructively covered. Medicine in Ancient Egypt, Ancient Persia, China, Japan, and early Greek Medicine receive satisfactory consideration. The Chapter on "Roman Medicine" (26 pages) is brief, but of interest. Mention is made of the edict by Numa Pompilus, king of Rome (C. A. 715 B. C.) in his "Leg Regia", ordering the performance of Caesarian section on women who died during labor.

Marcius Persius Cato (234-149 B.C.) agriculturist, censor, author of "De Rustica"—in which Cato recommended many remedies—urged the use of cabbage. He gave cabbage raw and cooked, and injected the juice into sinuses and fistulas by means of a syringe composed of a bladder tied to a reed. He advised mashed cabbage for ulcer or cancer. To-day, some investigators have recommended cabbage juice for peptic ulcer, and found that artificially produced ulcer in rats, rapidly heal under cabbage juice treatment. Modern writers have failed to give credit to Cato.

The author presents Galen in Chapter 29, (27 pages)—in a most interesting manner. Talmudic medicine—diagnosis and treatment, is done expertly and most satisfactorily in Chapters 30 and 31 (68 pages).

This book is highly recommended to all those who are historically minded, and particularly, to those physicians, scholars, and students interested in the history of medicine. All libraries should have copies available for their readers.

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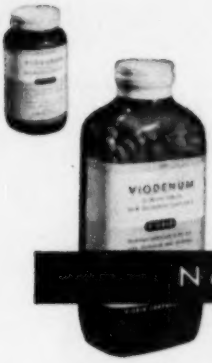

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*Streicher, M. H. F., Grossman, M. I., and Ivy, A. C., Gastroenterology, **12**, 371 (1949)

*Raimondi, P. J., Goetzl, F. R., Permanente Foundation Medical Bulletin, **7**, 1 (1949)

Gill, A. M., Lancet, **2**, 202 (1945); Proc. Roy. Soc. Med., **39**, 517 (1946)

Rivers, A. B., Am. J. Dig. Dis., **2**, 189 (1935)

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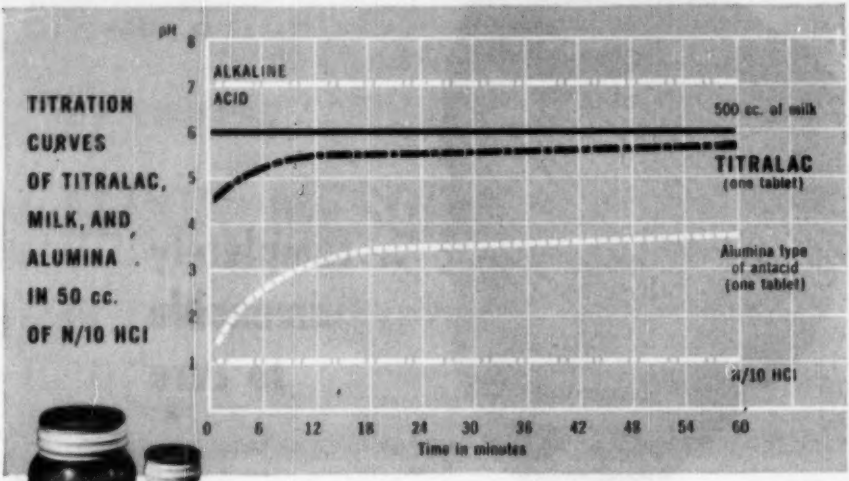

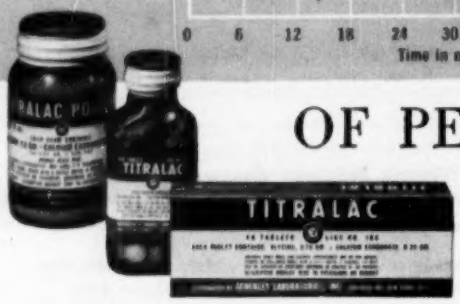

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REFERENCES

1. Rossett, N. E., and Flexner, J.: Ann. Int. Med. 18: 193 (1944). 2. Freezer, C. R. E.; Gibson, C. S., and Matthews, E.: Guy's Hosp. Reports 78: 191 (1928). 3. Aaron, A. H.; Lipp, W. F., and Milch, E.: J. A. M. A. 139: 514 (Feb. 19) 1949. 4. Kirsner, J. B., and Palmer, W. L.: Illinois M. J. 94: 357 (Dec.) 1948. 5. Kimball, S.: in Practice of Medicine (Tice). Hagerstown, Md., W. F. Prior Company, Inc., 1948; p. 210. 6. Special Article: M. Times 76: 10 (Jan.) 1948.

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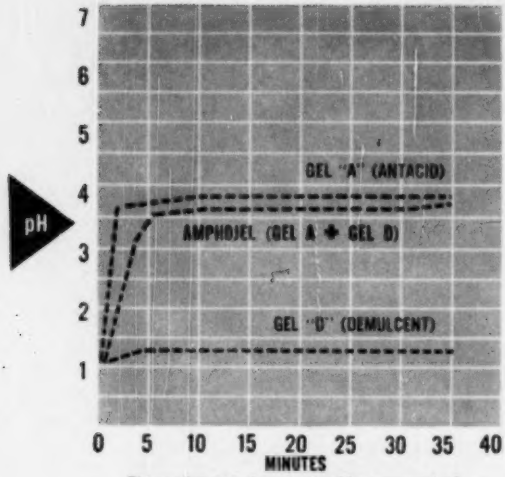

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